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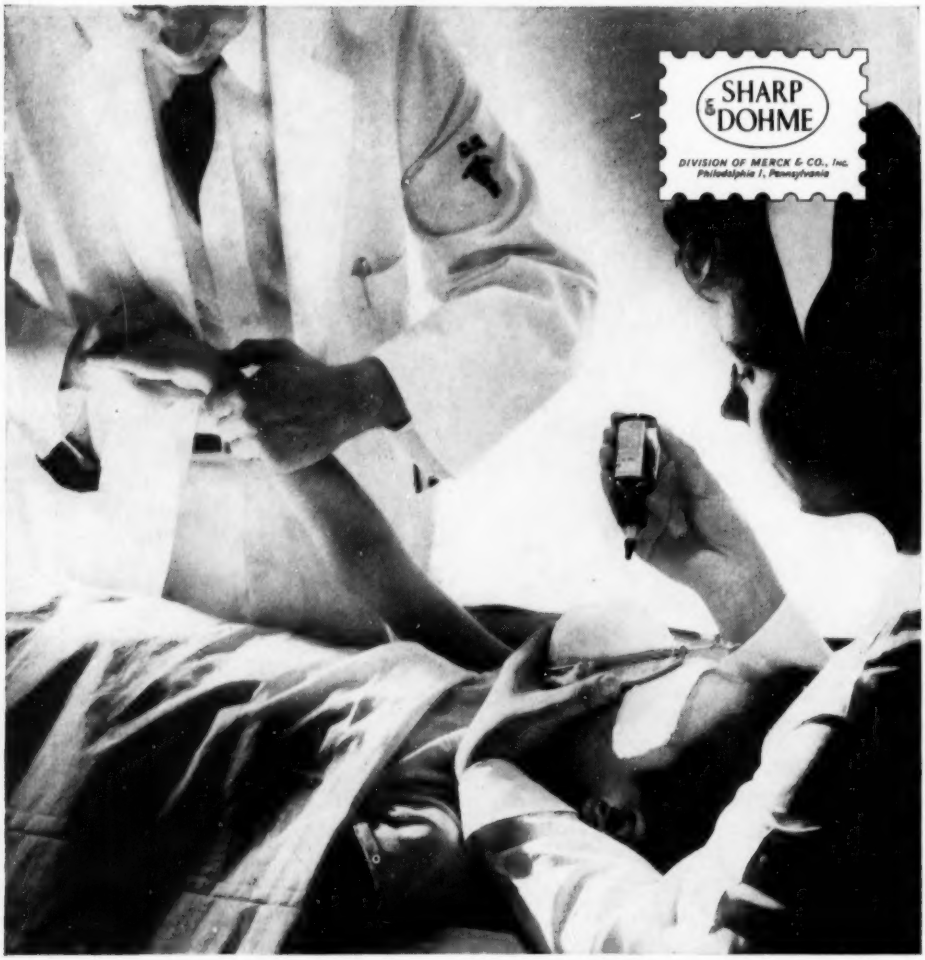

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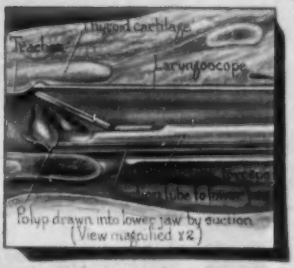
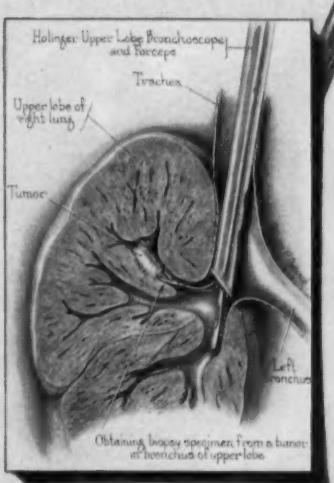


Illustration shows a polyp drawn by suction into lower jaw of Broyles laryngeal suction forceps.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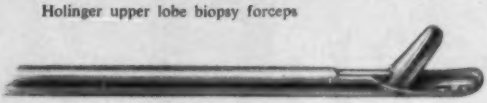

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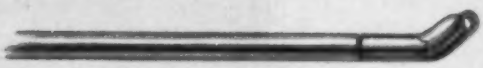

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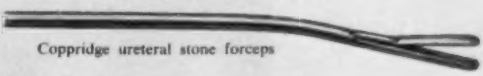

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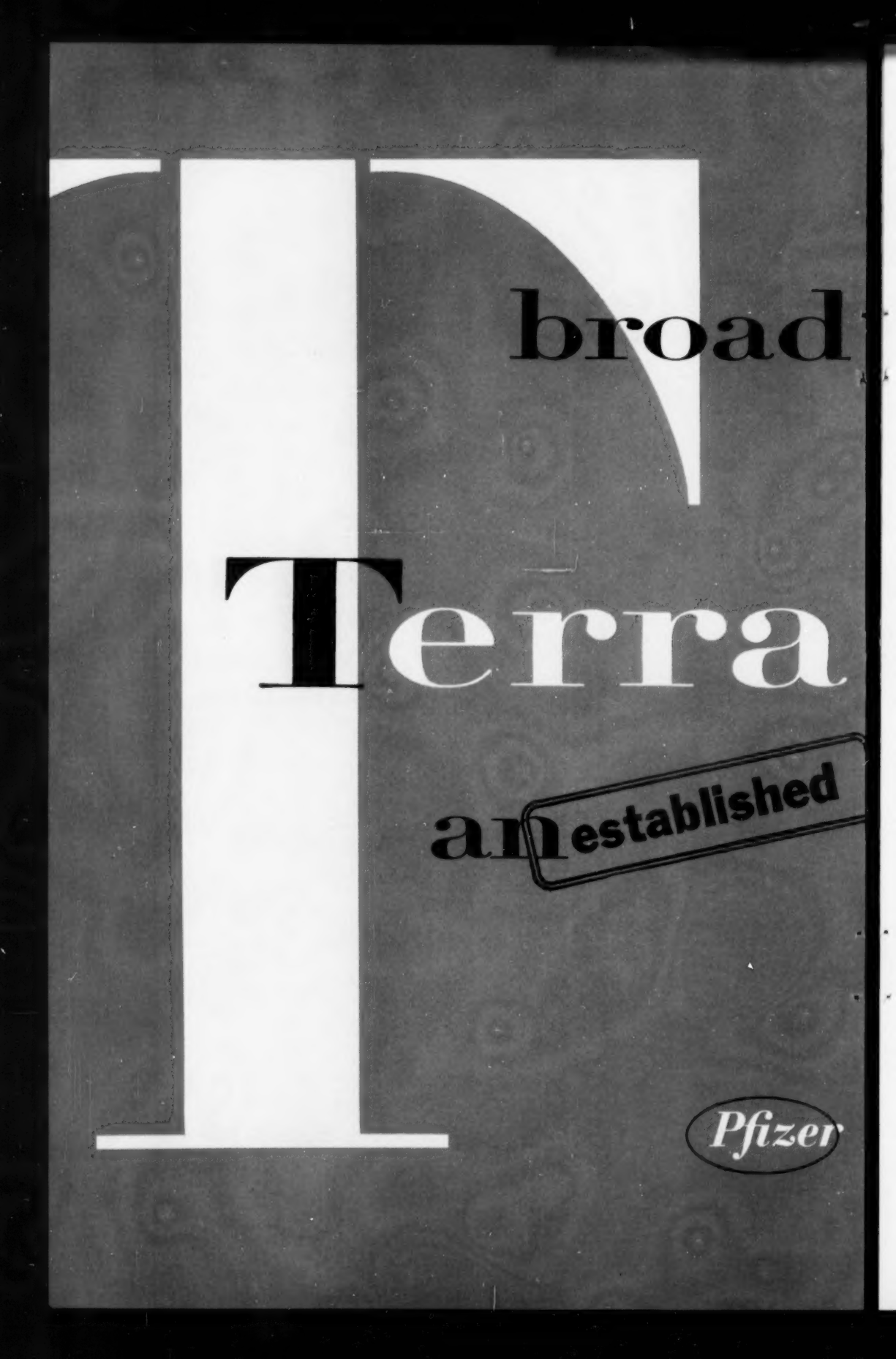
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Editorials

BASIC MECHANISMS IN UROLITHIASIS

THOUGH the mechanism of urinary calculus formation remains imperfectly understood, a number of contributing factors have been clearly established as important. Some of these factors can be simply demonstrated in experiments using rats with a surgically inserted foreign body in the bladder.[1] The foreign body serves as a uniform stimulus to stone formation, for such rats, even though maintained on a normal diet, consistently form a stone about the foreign body. In controlled experiments, if one or another of the supposed etiologic factors is removed, its significance becomes manifest in any difference in the weight of stone produced. By this method, the all-important factor of urinary concentration can be clearly demonstrated in several different ways. By inducing diuresis,[2] urinary dilution may become so great that stone formation no longer occurs. Stone formation is also completely prevented by reduction in the dietary intake of a single ionic component of the stone-forming crystalloid.[3] Likewise, a change in urinary pH with increased solubility of the stone-forming crystalloid will inhibit stone production.[4] Experiments of this type clearly illustrate that stone formation cannot occur if, for one reason or another, precipitation does not occur.

Urinary infection is ordinarily considered to be an extremely important factor in clinical urolithiasis. A number of experiments in rats on the role of infection in foreign body stone formation have yielded some unexpected findings.[5] While certain infections markedly augment stone production, others have no such effect. Some types of infection are actually inhibitory by mechanisms not as yet clear. The mechanism of stone augmentation by certain infections is also unknown. Only in instances of urea-splitting infection, in which marked stone production occurs, do we have a satisfactory explanation in that these infections result in a highly alkaline urine thus increasing precipitation. When considering the role of infection, a distinction should be made between its influence on stone genesis as over against stone augmentation or continued growth. Infection quite possibly is important in producing the initial lesion that sets off the process (stone genesis) but has little to do with the amount of stone formed thereafter. The rat experiments have little or nothing to say on the former possibility, since the foreign body already provides an adequate stimulus for stone initiation or genesis.

Recently there has been a renewed interest in the significance of what might be called urinary "solubilizers." By "solubilizers" is meant any substance which increases the solubility of the urinary crystalloid beyond its solubility in distilled water. Several mechanisms for "solubilizing" are available in the urine and at least

partially explain how urine may be excreted as a supersaturated solution.* For instance, the presence of magnesium ions increases the solubility of calcium oxalate and the magnesium ion in this instance might be considered as a "solubilizer." Another type of solubilizing activity is seen in the formation of complex ions such as the complex formed by calcium and citrate. Preliminary experiments indicate that complexing of this type does occur to some extent in human urine. The urinary calcium is, in part at least, bound calcium. Perhaps another type of "solubilizing" is found in the effect of urinary colloids. A small amount of nondialyzable colloidal material is, indeed, found in normal urine, but many efforts to demonstrate the influence of these materials on precipitation have led to conflicting results. Interest has been stimulated in this aspect of the problem by the report that injection of hyaluronidase subcutaneously results in marked colloidal change in the urine. This report has led to the widespread use of hyaluronidase as a stone preventer, but the clinical observations so far reported are not convincing. Using the foreign body technique in rats, controlled experiments completely failed to demonstrate any benefit by hyaluronidase treatment.[6]

When one tries to formulate a comprehensive scheme of the mechanism of stone formation, it becomes clear that there is no single cause for the disease, for many factors are significant. It is useful, then, to look on stone formation as a process requiring the simultaneous presence of several conditions. First, some degree of precipitation is absolutely necessary if a true stone is to form. Precipitation, in turn depends upon urinary volume, urinary pH, total crystalloid output, and the presence or absence of urinary "solubilizers." In addition to precipitation, it is obvious that at least some of the precipitate must be retained in the urinary tract if a stone is to form. Precipitate retention is furthered by the presence of any foreign surface to which precipitate may adhere, such as stones already present, foreign bodies, or the pelvic epithelial plaques which Randall considers a most important precursor of renal calculi. Likewise all structural abnormalities leading to urinary stasis predispose to stone formation by favoring retention of precipitate in the same manner. However, a stone is not an unorganized aggregate of retained crystals. A third basic condition must be added—that of stone matrix, binding substance, or scaffolding material. Unfortunately, very little is known of stone matrix, but its importance is shown in the extreme organization and complexity of the microscopic structure of stones, a condition presumably due to the stone matrix component.

We may, perhaps naively, set up the mechanism of stone formation as a chemical equation thus:

$$\text{Precipitate} + \text{Retention of ppt.} + \text{"Matrix"} \rightarrow \underset{\text{or incipient stone}}{\text{Stone}}$$

The question may be asked: Is this chemical reaction a reversible one? There is surprisingly meager evidence in the literature on dissolution of stones. Even in cases in which stones are said to have dissolved, doubt always remains as to whether or not the stones had passed spontaneously instead of dissolving. Clear evidence of dissolution has been obtained in experiments with rats using the foreign body technique. Preformed stones have been dissolved by chronic diuresis, acidification of

* Vermeulen, C. W.; Miller, G. E.; Chapman, W. H., and Finlayson, B.: Unpublished data.

the urine, reduction in concentration of one of the ionic components of the stone-forming crystalloid, and even by certain specific infections. In many instances, the stones dissolved completely, so that the foreign bodies were again free of any stone deposit and lay bare in the bladder at the end of the experiment. These experiments are taken as a conclusive demonstration that the reaction leading to stone formation is not an irreversible process and thus support the hope that ultimately many patients with urolithiasis may be treated by nonsurgical means.

C. W. VERMEULEN, M.D.

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COMBINED VAGUS RESECTION AND PARTIAL GASTRECTOMY FOR DUODENAL AND MARGINAL ULCER

LOUIS T. PALUMBO, M.D.
THEODORE T. MAZUR, M.D.
AND
BERNARD J. DOYLE, M.D.
DES MOINES, IOWA

IN JULY, 1947, we initiated a program of combining a partial gastrectomy with a bilateral infradiaphragmatic vagus resection in the surgical treatment of duodenal or marginal ulcer. It was our purpose to determine whether the addition of vagectomy could improve our over-all results of partial gastrectomy and make it a practical supplement in future surgical therapy. At that time, the assumption was, first, that the addition of vagus resection might, because of postoperative

TABLE 1.—*Age Distribution*

Age	No.	%
20-29	7	17
30-39	10	24
40-49	5	11
50-59	16	38
60-69	4	10
	42	100

persistent achlorhydria, result in the elimination of postoperative marginal or stomal ulcer; second, that it might, because of the delayed emptying time of the gastric remnant, result in reducing the incidence and severity of the dumping syndrome, and, third, that if both the aforementioned factors could be modified by such a procedure, this combined procedure might, at a future date, permit with safety a less radical gastric resection, thereby allowing for a larger gastric pouch, which would eliminate the necessity of frequent small feedings.

This combined procedure was employed, and since the inception of our study is being carried out, in other groups, centers, or clinics in this country.*

PURPOSE

It is the purpose of this study to present the findings and results of 42 cases treated by this method during a six-year period beginning in July, 1947.

From the Department of Surgery, Veterans Administration Hospital.

* References 1 to 10.

AGE INCIDENCE

The patients ranged in age from 24 to 65 years; the average age was 42 years. The greatest number was in the 30- to 39- and in the 50- to 59-year age groups.

The average duration of symptoms was 9 years, and the interval of time between previous surgery and this definitive surgical procedure was 66 months. Thirty-eight per cent of the group had previous surgery (Table 2).

TABLE 2.—*Previous Surgery*

Type	No.	%
Gastrectomy, partial	1	2
Gastroenterostomy	3	7
Perforation, ulcer, closure of	12	29
Totals	16	38

TABLE 3.—*Complication Prior to Definitive Surgery*

Type	No.	%
Hemorrhage	25	60
Minimal	9	
Moderate	11	
Severe	5	
Obstruction, pyloric	16	38
Mild	8	
Moderate	4	
Severe	4	
Pain and intractability	9	21
Perforation	12	29

TABLE 4.—*Frequency of Gastrointestinal Bleeding*

Age	Number of Times Patient Bled				
	1	2	3 or More	Total	%
20 to 29	4	1	2	7	28
30 to 39	4	2	1	7	28
40 to 49	0	1	2	3	12
50 to 59	2	2	3	7	28
60 to 69	0	1	0	1	4
Totals	10 (40%)	7 (28%)	8 (32%)	25	

COMPLICATION OF ULCER PRIOR TO SURGERY

Many of these patients had a combination of complications resulting from their ulcer syndrome. These are listed in Table 3, which reveals that the most frequent types were bleeding (60%) and/or obstruction (38%).

GASTROINTESTINAL BLEEDING

Preoperative gastrointestinal bleeding occurred in 25 (60%) of the patients. It was considered massive in 5 (12%), moderate in 11 (26%), and minimal in 9 (21%). The massive hemorrhage occurred in 22.7% of the patients under 50 years of age and in only 5% of the patients over 50. Emergency or interval gastrectomy was performed in four of the five patients with massive hemorrhage.

Sixty per cent of the patients had a history of repeated episodes of bleeding. Seventy-seven per cent of the cases of bleeding occurred in patients under 49 years of age (Table 4).

PREOPERATIVE GASTRIC ANALYSES

Preoperative gastric analyses were carried out in all patients except those actively bleeding or those who had marked pyloric obstruction. In 94% of the patients in whom a Hollander's (hypoglycemic) insulin test was made, more than 50 units of free acid was found. The cephalic phase of secretion of free acid was definitely augmented. The average 12-hour volume of resting night secretion was 830 cc.; in 60% of the cases studied the night secretions were 1,000 cc. or more.

TABLE 5.—*Postoperative Complications**

Type of Complication	No. and %
Wound	
Abscess	2
Hematoma	1
	3 (7%)
Pulmonary	
Atelectasis	3
Effusion, pleural	1
	4 (9.5%)
Other complications	
Atony, gastric	6
Bleeding, gastric	1
Diarrhea and distention	2
Jaundice, homologous serum	1
Leak, duodenal stump	3
Obstruction, efferent stoma	3
Obstruction, intestinal, transient	1
Pericardial, effusion, traumatic	2
	19 (45%)

* There were no eviscerations or postoperative incisional hernias.

OPERATION

Partial gastrectomy, removing about 75% of the stomach, was performed through a transverse, elliptical, transrectus, supraumbilical incision. An antecolic gastrojejunal anastomosis, with a short afferent limb, was performed. In all cases the duodenal ulcer, associated fibrosis, or marginal ulcer was resected. A bilateral vagus resection was accomplished below the diaphragm after mobilization of the lower esophagus through the esophageal hiatus. All of the vagal fibers were divided, with removal of at least 2 to 4 in. (5 to 10 cm.). All of the abdominal incisions were closed with interrupted fine nonabsorbable surgical (silk) sutures. The majority of the patients were ambulatory on the first postoperative day.

RESULTS

Forty-two patients were operated upon; of this number 35 (83%) were followed for a period of 6 to 78 months. The average follow-up was 43 months; however, 74% were followed more than 3 years. In the majority of cases, a biannual follow-up was carried out; at yearly intervals the patient was admitted

to the hospital for detailed studies. Of the remaining 7 patients of the original group of 42, 1 died after surgery and 6 were lost, owing to change of address or failure to return for follow-up studies.

Postoperative Complications.—There was a total of 26 postoperative complications, which occurred in 14 (33%) of the patients. Of this number, 4 (15%) were pulmonary, 3 (11%) involved the wounds, and the remaining 19 (74%) were varied (Table 5).

Postoperative Deaths.—There was 1 (2.4%) death in this series of 42 cases. The cause of death was peritonitis due to perforation of the duodenal stump.

TABLE 6.—*Results of Follow-Up Studies of Thirty-Five Cases*

		No. of Cases
Weight		
Gain		14 (42%)
Loss		14 (42%)
No change		6 (16%)
Dumping Syndrome		7 (20%)
Mild	3	
Moderate	3	
Severe	1	
Bowel Change		
Diarrhea		9 (21%)
Severe	4	
Occasional	5	
Diet		
Regular		22 (63%)
Restricted		13 (37%)
Marked restriction	2 (6%)	
Mild restriction	11 (31%)	
Frequency of Feedings		
3 times daily		22 (63%)
3 to 5 times daily		5 (14%)
More than 5 times daily		8 (23%)
Pain		
Ulcer-like pain		1 (3%)
Distress with overindulgence		6 (17%)
No pain		28 (80%)
Ability to Work		
Good		22 (63%)
Fair to good		4 (11%)
Poor		3 (8.5%)
Unable to work (cardiac, retired, etc.)		6 (17.5%)

Postoperative Gastric Analyses.—These studies were carried out in 29 patients. On repeated analyses of the gastric secretions of the fasting stomach and after histamine, no free hydrochloric acid was found. Hollander's insulin test (hypoglycemia) did not produce free acid in any of the cases. This anacidity or achlorhydric state existed in all the patients studied, even those followed as long as six years. From this finding it can be assumed there was no evidence of regeneration of the vagus pathways and that the cephalic neurogenic phase of secretory stimulation was eliminated.

The 12-hour volume of the resting gastric night secretions was reduced to an average of 360 cc., as compared to an average of 830 cc. prior to surgery.

Postoperative Gastrointestinal Roentgenographic Studies.—Such examinations made shortly after surgery revealed gastric atony and dilatation with delayed emptying time of the gastric remnant, which averaged three hours in this group. However,

after a period of six months or longer, there was evidence of return of gastric tone. Late follow-up studies revealed the emptying time of the gastric remnant to be normal in 90% of the cases and delayed in the remaining number.

Repeated barium motor meal roentgenographic studies of the small bowel were carried out in 28 patients. These studies revealed in 60% of the cases no dysfunction of the small bowel. The small bowel pattern and motility were considered within normal limits, whereas in 11, or 40%, of the cases studied, the small bowel pattern revealed clumping, segmentation, and hypomotility, with delayed transit time. These motor meal pattern changes are similar to those found in regional enteritis. In only three cases were the patient's symptoms related to these bowel changes.

EVALUATION OF FOLLOW-UP STUDIES

After operation 42% of the patients gained weight, whereas the same number lost weight, and in the remaining number there was no change. The dumping syndrome occurred in 20% of the cases. The greatest disturbance occurred in bowel function, with 21 per cent developing a diarrhea which persisted, and in one-half of this group it was considered severe.

Two-thirds of the patients were on an unrestricted diet with three meals a day. The remaining number required more feedings daily and were on a dietary regimen. Eighty per cent were free from pain and the peptic ulcer syndrome. In 17% of the patients, various gastrointestinal disturbances occurred with dietary overindulgence (Table 6).

Marginal or stomal ulcers did not develop in any patient in this series.

In the over-all evaluation of the results in the 36 patients in which adequate follow-ups were obtained, 32 (80%) were considered satisfactory.

COMMENT

The addition of bilateral infradiaphragmatic vagus resection to partial gastrectomy did not increase the mortality but did introduce an additional surgical hazard and did increase the morbidity rate. Mobilization of the esophagus in two instances may have been responsible for the pericardial effusion, which we thought was on a basis of direct trauma.

The over-all results were satisfactory in a large percentage of the cases and were almost comparable to those in which only partial gastrectomy was performed. However, the patients who were classified as unsatisfactory had complaints and physiological disturbances which were severer and of greater magnitude than a comparable group without a vagus resection. This was particularly evident in the disturbances due to impaired gastrointestinal motor function, such as delayed emptying time of the gastric remnant and the disturbance of bowel function characterized by diarrhea and/or alternating diarrhea and constipation.

The addition of vagus resection to date has prevented marginal or stomal ulcer formation. This most likely is due to the persistent achlorhydria which exists in all these patients. This state of anacidity exists not only in the fasting stomach but after histamine and the Hollander insulin tests. Apparently, this indicates in this series that all the vagal pathways to the stomach were divided during surgery and that the division was of such scope that regeneration or reestablishment of the pathways was impossible.

In this connection it is important to note whether or not this state of persistent achlorhydria will be a factor which may have undesirable sequelae after 10 to 20 years, for a high per cent of the malignant conditions of the stomach are associated with persistent achlorhydria, too.

The incidence of the dumping syndrome was not reduced by this combined procedure, in spite of the delayed emptying time of the gastric remnant.

It appears to date that the combining of these procedures has (1) eliminated marginal or stomal ulcer from developing, (2) has not reduced the incidence of or eliminated the dumping syndrome, and (3) has created other physiological disturbances and sequelae which are more troublesome than those following resection alone.

In view of these studies, it is the opinion of one of us (L. T. P.) that this combined procedure would permit a less radical gastric resection in which only the gastric antrum is removed, thereby allowing for a larger gastric pouch, which would eliminate the necessity for frequent feedings. With anacidity, which may result in practically all the cases, marginal ulcer formation would be unlikely in this group. A more logical approach, if it were technically possible, in most cases, would be to divide the entire left vagus and its branches and only the gastric branches from the right vagus below the diaphragm. By so doing, we might eliminate many of the undesirable physiological sequelae, such as diarrhea and other motor-digestive disturbances of the gastrointestinal tract. With the main trunk of the right vagus left intact, the motor and secretory portions of this nerve to the duodenum, pancreas, small bowel, and at least the right half of the colon would not be disturbed. Destruction of these pathways does not contribute anything in the elimination of the peptic ulcer syndrome per se.

During the past several years our policy has been to use this combined procedure only in those patients who exhibit a severe form of emotional instability, anxiety state, and disturbance in their autonomic nervous system stability. By careful observation of these patients and by means of the Hollander insulin test, we can easily select the patients we feel require this type of procedure. With evidence of an augmented cephalic phase of gastric secretory function or activity, as shown by a high response following a Hollander insulin test in these patients, it is our opinion, in order to prevent marginal or stomal ulcer that this combined procedure is necessary to produce a state of achlorhydria.

SUMMARY AND CONCLUSIONS

The results of a combined procedure of partial gastrectomy with a bilateral infradiaphragmatic vagus resection for the treatment of duodenal or marginal ulcer in 42 consecutive men patients is presented.

The combined procedure did not increase the mortality rate but did increase the morbidity rate and resulted in a greater number of undesirable physiological sequelae than in the group in which partial gastrectomy alone was done.

The combined procedure to date has not resulted in any marginal or stomal ulcers. This is most likely due to the achlorhydria which has occurred and has persisted in all cases.

The incidence of the dumping syndrome was not reduced in this group. In more than one-third of the patients, roentgenographic studies of the motor activity of the small bowel revealed abnormalities characterized by hypomotility, clumping, segmentation, and puddling of the barium column.

In view of the persistent achlorhydria in all cases, it is our opinion that a combined procedure of this type could be performed in which a less radical type of gastric resection could be accomplished without the risk of marginal or stomal ulceration.

Since the over-all results in our hands are not as good as those in which only a partial gastrectomy is performed, it has been for several years, and it is now, our policy to adopt the combined procedure only in those patients who have a high cephalic phase of acid secretory function and who also exhibit evidence of autonomic nervous system instability.

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BOECK'S SARCOID OF THE STOMACH SIMULATING LINITUS PLASTICA

Report of a Case and Comparison with Twelve Recorded Cases

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BOECK'S sarcoid frequently involves the lymph nodes and the lungs, but involvement of the stomach is rare. The case to be presented and the 12 others culled from the literature (Table) are of interest because in each instance symptomatology and barium studies mimicked gastric ulcer or carcinoma.

Jessing,[1] in 1943, described the case of a 61-year-old white woman who suffered from epigastric pain, belching, and vomiting of three weeks' duration. An ulcer was seen on the lesser curvature in the barium study. This lesion persisted, and because a malignant tumor was feared, laparotomy with subtotal gastric resection was undertaken. An ulcer 2 cm. in diameter with an infiltrating rim was found. The gastric wall was greatly thickened, and the mucosa had a velvety appearance.

In 1944, Gore and McCarthy[2] published their study of a 26-year-old man who complained of burning epigastric pain and eructation after meals. A cone-shaped deformity of the antrum was seen on the roentgenogram, prompting the diagnosis of an infiltrating carcinoma. However, examination of the resected specimen showed a thickened, doughy stomach wall with an ulcer on the lesser curvature. These pathologic changes were due to Boeck's sarcoid.

In 1947, Guibert[3] reported the case of a 61-year-old woman who, it was believed, had a gastric carcinoma because of epigastric distress, anorexia, weight loss, and a lesser curvature ulcer, demonstrated by x-ray studies. The stomach was subtotally resected, and the correct diagnosis was made from histopathologic study of sections taken from the ulcer area. In the same year, Oppenheim and Pollack[4] described the case of a patient who had undergone subtotal gastric resection six years previously because of persistent epigastric pain and a lesser curvature ulcer. Review of the sections showed the pathology to be due to Boeck's sarcoid.

Garcia Moran,[5] in 1948, recorded the case of a 34-year-old white man who had suffered for 15 to 20 days with heaviness in the epigastrium which became worse after eating and was not relieved by vomiting. Roentgenologic study showed a persistent deformity in the antrum. At laparotomy the surgeon was surprised to find a universal thickening of the gastric wall, which had the consistency of leather and was diffusely reddened. The surgeon did not believe that it was a carcinoma, and so only a biopsy was done. The slides were reviewed and a final diagnosis of sarcoid was made. The patient improved under roentgen therapy.

Orie, van Rijssel, and van der Zwaag,[6] in 1950, reported a similar experience with a 53-year-old woman, who complained of postprandial nausea and vomiting

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Case Summary of Pertinent Data

Authors	Age; Race Sex	Symptoms	Duration of Illness	Wt. Loss	Laboratory Data: Free HCl	Laboratory Data: Serology	Laboratory Data: Anemia	Roentgenologic Findings	Appearance of Stomach at Operation	Other Organ Involvement
Jessing [1]	61 White F	Epigastric pain	3 wk.	.....	+	Neg.	0	Lesser curvature ulcer	Lesser curvature ulcer; gastric wall and mucosa greatly thickened	None
Gore and McCarthy [2]	26 M	Burning in epigastrium; eructation after meals	18 mo.	18 lb.	0	+	+	Cone-shaped deformity of antrum	Greater curvature deformity of antrum	Regional lymph nodes
Guibert [3]	61 White F	Dull pain with exacerbations	5 yr.	"Marked"	..	Neg.	0	Lesser curvature ulcer	Gastric ulcer	Regional lymph nodes
Oppenheim and Pollock [4]	50 White F	Generalized epigastric distress	12 mo.	.....	..	....	..	Lesser curvature ulcer	.....	Lymph nodes and liver
Garcia Moran [5]	34 White M	Heaviness in epigastrium, worse after eating, remains after vomiting	15-20 days	.....	0	....	..	Irregularity in pyloric antrum	Greatly thickened gastric wall; mucosa reddened	Regional lymph nodes; parotids, conjunctiva
Orie and others [6]	53 F	Nausea and vomiting after meals; anorexia	12 mo.	.....	0	....	+	Narrowing of ½ pyloric antrum	Greatly thickened gastric wall; narrowed pylorus	Regional lymph nodes, lungs (generalized disease)
Appell and others [8]	48 White F	Postprandial fullness and eructation; could take only liquid and soft diet	12 mo.	32 lb.	0	Neg.	0	Pyloric obstruction with gastric dilatation	Wall of pyloric area thickened; mucosa reddened	None
Comfort and others [7]	22 M	Severe pain, l. u. q., with nausea and vomiting, later diarrhea	36 mo.	12 lb.	0	....	+	Duodenal ulcer; later stenosis of 2d and 3d parts	Wall thickened at pylorus; ulcers and nodular hyperplasia of mucosa	Duodenum; jejunum; ileum
	49 M	Pressure in epigastrium; fullness after eating; diarrhea	36 mo.	35 lb.	0	....	+	Constriction 1st and 2d parts of duodenum	Ulcerations and inflammatory reaction at pylorus	Duodenum; jejunum, and omental nodes
Bauer [9]	59 Negro F	Postprandial epigastric distress	12 mo.	45 lb.	0	Neg.	0	Antral defect	Wall of distal half thickened; mucosa nodular; papillary lesion in antrum	None
McKusick [10]	49 White M	Heaviness; gaseous eructation post cibum	24 mo.	114 lb.	0	Neg.	0	Linitus plastica appearance	Mucosa darkened; no rugae	Regional lymph nodes
	41 White F	Recurrent massive upper G. I. bleeding; frequent diarrhea	12 mo.	None	..	Neg.	..	Normal appearance (?)	3 or 4 superficial ulcers	None
Author	27 White M	Postprandial nausea and vomiting; epigastric pain	3 mo.	30 lb.	0	Neg.	0	Rigid appearance, coarse folds (linitus plastica)	Entire wall greatly thickened; mucosa reddened	Pancreas; lymph nodes; liver; parotids

of 12 months' duration. After vomiting the patient noted pain in the epigastrium. For several years previously, she was thought to have tuberculosis because of a diffuse, patchy pulmonary infiltrate; however, her sputum and the tuberculin test were repeatedly negative. At one time, seven years earlier, a pancreatitis was diagnosed during laparotomy undertaken for investigation of persistent abdominal complaints. The roentgenogram showed a constant antral narrowing. The preoperative diagnosis was pulmonary sarcoidosis and antral carcinoma. At laparotomy the antrum was found to be diffusely thickened and rigid, and so a partial gastrectomy was performed.

The same year, Comfort and associates [7] described two cases in which a diagnosis of regional enteritis had been made because the duodenum, jejunum, and ileum were also involved and the patients suffered from bouts of diarrhea. However, the findings in both cases were histopathologically compatible with the diagnosis of sarcoidosis of the stomach.[10] Their first patient, a 22-year-old white man, had suffered from burning pain in the left upper quadrant for two years. The barium studies were interpreted as showing stenosis of the second and third parts of the duodenum. At operation the walls of the stomach, pylorus, and duodenum were seen to be markedly thickened and edematous. The pylorus was patent, but there was a constriction just distal to the ampulla of Vater. The gastric mucosa was involved with ulcerations and nodular hyperplasia. A biopsy and posterior gastroenterostomy were done. Their second patient, a white man aged 49, had been having a sense of pressure and fullness in the epigastrium for three years. The x-ray showed a constricting deformity in the first and second parts of the duodenum. The surgeon found the gastric wall to be thickened and the mucosa ulcerated. The deformity seen on the x-ray was also noted. As in their first case, a biopsy and posterior gastroenterostomy were done.

The patient reported in 1951 by Appell, Pritzker, and Klotz [8] was a 48-year-old white woman who had been suffering from nausea, vomiting, and weight loss. She was able to take only liquid nourishment. The roentgenologic examination showed a pyloric obstruction with a greatly dilated stomach. No ulcer was seen. At the time of resection, the stomach was found to be dilated and to have a very thickened wall. The lesion was located in the prepyloric area; the pylorus would admit only the tip of the little finger, and the mucosa was reddened and thrown up into coarse folds.

Bauer,[9] also in 1951, described an unusual case in which gastric sarcoid coexisted with a papillary carcinoma of the stomach. The carcinoma was located proximally in the antrum and was separate and distinct from the sarcoid lesions which were situated more distally, at the pylorus. This patient was a 59-year-old Negro woman who had been suffering for one year with epigastric discomfort and gaseous eructation after eating. Barium studies demonstrated a filling defect in the antrum. The wall of the distal half of the stomach was thickened, and near the pylorus the mucosa was hypertrophied and nodular. Proximal to this there was a polypoid lesion. A subtotal gastric resection was performed. The patient, when seen two years later, appeared to be doing well.

Recently, McKusick [10] reported two cases of gastric sarcoid. One was that of a 49-year-old white woman who complained of heaviness in the upper abdomen and gaseous eructation, relieved by vomiting. These symptoms were of two years' duration, and during this period she had lost 114 lb. (51.7 kg.). At laparotomy

the distal half of the stomach was found to be thickened, and there were nodular areas beneath the serosa suggestive of tumor implants. The mucosa was dark red. A subtotal gastrectomy was performed. The second case was that of a white woman, aged 41, who had had two episodes of hematemesis. Fluoroscopy demonstrated prominent gastric rugae, and at one time a lesser curvature ulcer was reported. Because the patient dreaded the prospect of further massive hemorrhages, laparotomy was performed. Superficial ulcerations were found in the gastric mucosa, and a resection was performed.

REPORT OF CASE

J. W., a 27-year-old white man, had suffered from postprandial projectile vomiting for three months prior to admission. The patient complained of cramping epigastric pain that appeared

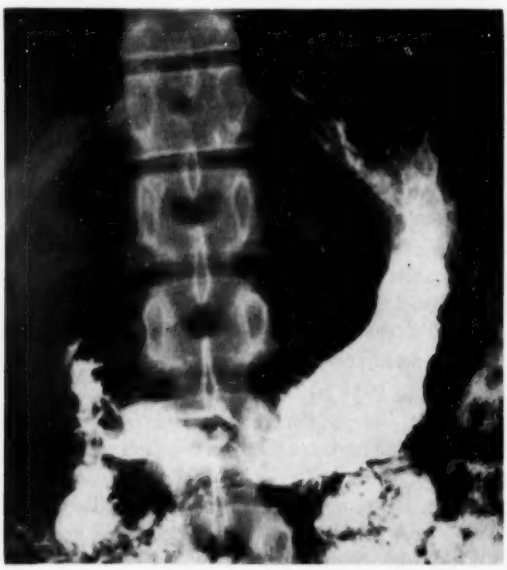

Fig. 1.—Roentgenogram showing coarsened folds and rigid appearance of stomach.

after the ingestion of more than "one pint of food or liquid." The pain was relieved by eructation. He did not experience anorexia but had lost 30 lb. (13.6 kg.) in the three-month period preceding his admission. A single bout of diarrhea had occurred during the week immediately following the onset of the illness.

On physical examination, he was found to be thin but did not appear acutely ill. There was tenderness in the epigastrium just to the left of the midline. Both parotid glands were markedly swollen but were nontender.

The red blood cell count was 4,850,000, with 14.2 gm. of hemoglobin per 100 cc. The total protein was 5.9 gm. per 100 cc., with an albumin-globulin ratio of 3.9:2.0. There was no free acid in the stomach. The stools were repeatedly guaiac-positive, and the serology was negative. Roentgenologic examination of the stomach showed coarsened mucosal folds and rigidity of the gastric walls (Fig. 1). During fluoroscopy, no peristalsis was seen, and emptying was delayed.

The preoperative diagnosis was carcinoma of the stomach of the linitus plastica type. At laparotomy the entire stomach appeared to be diffusely inflamed. The wall was thick and rubbery in consistency. When the stomach was opened, the mucosa, particularly in the distal half,

was seen to be reddened and greatly thickened. These changes extended into the first part of the duodenum. No mechanical obstruction could be demonstrated. The pancreas was diffusely swollen, and nodular, and appeared to be involved by the same process; however, biopsy was thought not advisable. The gross appearance of the stomach was interpreted as being suggestive of a lymphoma or Hodgkin's disease rather than of linitus plastica, and a liberal full-thickness biopsy specimen was taken of the gastric wall. The pathologist reported "a granulomatous lesion resembling eosinophilic granuloma." In view of this, and because the outlet of the stomach appeared adequate, additional surgery did not appear indicated. Furthermore, the evidence of involvement of other viscera would have precluded a curative resection. Several regional lymph nodes and a piece of liver (in spite of its normal appearance) were removed for microscopic study. The patient's postoperative course was uneventful.

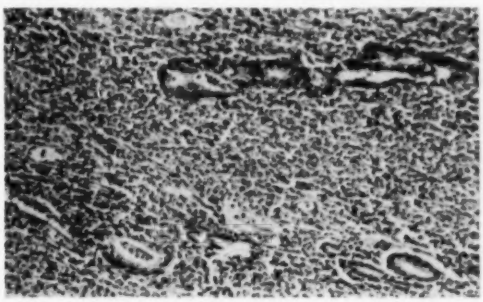

Fig. 2.—Section of stomach wall showing reticulum cell infiltrate of gastric mucosa and submucosa; × 60.

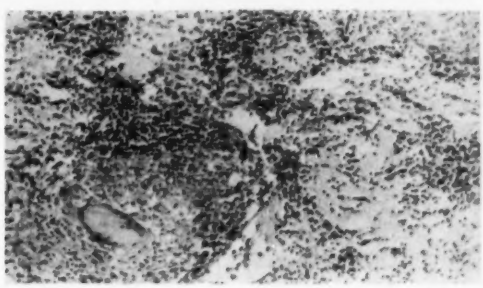

Fig. 3.—Section of lymph node showing typical tubercle, epithelioid and multinucleated giant cells. The paramyloid reaction is also present; × 75.

Subsequent microscopic examination of the permanent sections showed a remarkable infiltration of the gastric mucosa and submucosa by large cells having abundant pink-staining cytoplasm and vesicular nuclei (Fig. 2). These cells were identified as reticulum cells or tissue monocytes. In several areas multinucleated giant cells of the Langhans type were present. Tubercles were not seen in the gastric mucosa, nor were there any areas of necrosis.

Multiple sections through the lymph nodes demonstrated the extensive replacement of the normal lymphoid tissue by innumerable tubercles, composed of reticulum cells, epithelial cells, and multinucleated giant cells of the Langhans type (Fig. 3). There was no central necrosis; however, in several of the nodes these granulomatous changes were associated with massive deposits of pink-staining material, which, in some areas, resembled amyloid. The liver biopsy specimen also contained similar granulomata (Fig. 4).

Because of the recent reports in which beneficial results have been obtained with cortisone in cases of sarcoidosis,* it was decided to place this patient on a course of 150 to 200 mg. daily. The patient, while on therapy, lost no weight and noted a regression of the parotid swelling. However, in a recent barium study obtained 10 months' postoperatively, there was no evidence of regression of the gastric and pancreatic involvement. The deformity of the stomach and the retrogastric mass were unchanged; involvement of the esophagus was strongly suggested. Also, there was evidence of beginning uveal tract involvement. The liver and spleen were still not palpable. The cortisone was then withheld, resulting in a prompt return of anorexia, with a weight loss of 5 lb. (2.3 kg.) in a month's time.

COMMENT

Other granulomatous lesions which have been found in the stomach by the pathology department were considered in making the histopathologic diagnosis of Boeck's sarcoid in this case. These included tuberculosis, syphilis, and eosinophilic granulomas; however, it is believed that the microscopic features described previously are sufficiently typical to warrant the diagnosis of Boeck's sarcoid. Nevertheless, the interpretation of the microscopic findings can be complicated, as Nadel

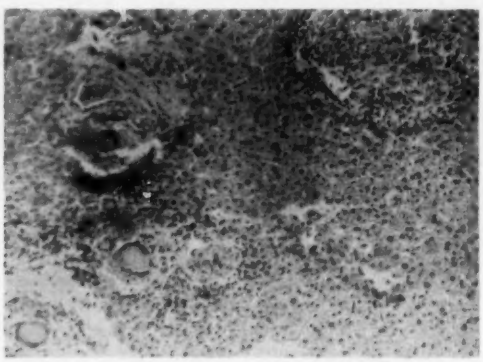

Fig. 4.—Section of liver showing granulomatous changes similar to those in lymph node; × 75.

and Ackerman [13] pointed out in their interesting paper. They reported five cases in which sarcoid-like lesions were found in lymph nodes that drained an area containing a malignant neoplasm, and so they stated that a distinction should be made between the "sarcoid lesion" and the disease entity proper.

Of additional interest in this case was the presence of hyaline deposits in the lymph nodes. This condition has previously been described by Teilum,[14] who termed it hyalinosis or paramyloidosis. He considered it a manifestation of an immunity reaction in reticuloendothelial tissue occurring in sarcoidosis and other diseases.

The ages of the patients with Boeck's sarcoid of the stomach varied as in the commoner forms. The youngest was 22, and the oldest, 61. Although in some patients other viscera were also involved with Boeck's sarcoid, each patient sought medical care because of symptoms related to the gastric lesion. The shortest period between onset of symptoms and medical consultation was 20 days; the

* References 11 and 12.

longest, 5 years. In most instances, symptoms of obstruction were prominent, varying from distress after eating to retching and vomiting. These may be attributed to the narrowing or constriction of the duodenum or pylorus or to the diffuse thickening of the gastric wall, with its consequent loss of motility.

Of all the laboratory tests, the absence of free hydrochloric acid in the gastric secretions was the only consistent finding. Jessing's case was the only exception encountered. The roentgenograms presented an appearance compatible with that of an infiltrating carcinoma in seven instances and of an ulcer in three. In only two patients was duodenal pathology noted, in one other the evidence was equivocal.

The treatment in nine cases consisted of subtotal gastric resection because of a mistaken diagnosis of carcinoma. In the other four instances the surgeon believed that the lesion was of some other type; in two of these gastroenterostomy (and biopsy) was done to by-pass a duodenal obstruction; in the remaining two biopsy alone was deemed sufficient. The main feature which aided in deciding against carcinoma in these four cases was the finding of an edematous, rubbery gastric wall, in contrast to the hard, rigid wall found in an infiltrating carcinoma of the linitus plastica type. The thick, reddened, velvety mucosa was also helpful.

Because Boeck's sarcoid is known to be protean in its behavior and frequently undergoes recession spontaneously, prognosis and evaluation of treatment are difficult. This disease has a long survival time. In a recent follow-up study of 194 patients with sarcoidosis, the 10-year survival rate was 80%.[15] One of the patients described in the foregoing paragraphs,[7] a 22-year-old man, was doing satisfactorily at the time of the report, 14 years after his gastroenterostomy. All the patients reported in this paper were treated symptomatically, except for Moran's patient, who received irradiation therapy over the upper abdomen postoperatively. However, the results of irradiation and the other forms of treatment previously recommended have been disappointing.[16] Cortisone has been reported to effect a temporary repression of symptoms, and perhaps to slow the progress of the lesion. A change in the histologic appearance of the lesion from a granulomatous process to a fibrous one has been noted.[17] However, it has been the general experience that when the cortisone is discontinued, exacerbations of the disease are prone to develop.

Whereas cortisone has been the chief therapeutic weapon in the management of the patient presented by this clinic, special attention has been given to the nutritional state and well-being of the patient. Accordingly, he has been instructed to select foods of high caloric value with low bulk in order to keep gastric complaints to a minimum while maintaining an adequate intake. Between-meal supplements or multiple equal feedings may be necessary to accomplish this.

SUMMARY

The case of a patient with gastric symptoms caused by involvement of the stomach by Boeck's sarcoid is reported. A review of 12 other such cases reported in the literature exhibiting symptoms and roentgenologic findings identical with those seen either in gastric ulcer or in linitus plastica is also presented. The present patient at the time of laparotomy presented an edematous, rubbery gastric wall with a reddened, velvety mucosa. These findings placed the diagnosis of carcinoma in doubt, and the stomach was not resected. Subsequently, after a diagnosis of Boeck's

sarcoid was established from histopathologic examination of the biopsy material, the patient was placed on cortisone therapy. Withdrawal of the cortisone for a month allowed the return of gastric complaints and loss of weight.

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SPLENOSIS

Review and Report of Subcutaneous Splenic Implant

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SPLENOSIS has been defined as autotransplantation of splenic tissue in the abdominal cavity following splenectomy or injury. Buchbinder and Lipkoff [5] proposed the term while reporting a case.

The first human case was reported by Albrecht [1] in 1896 and the second by Schilling [31] in 1907. It is of interest that these two are the only cases in the entire literature with no history of splenectomy or trauma. These authors, and Küttner,[20] who reported the third case in 1910, believed the peritoneal nodules to be accessory spleens. Albrecht's and Schilling's cases had adhesions around the diminutive main spleen, atrophy of the left kidney, and an irregularly shaped omentum. Albrecht postulated an intrauterine disturbance of the anlage of the organs in the left upper quadrant. Faltin,[7] reporting a case in 1911, was the first to believe that the nodules were splenic implants. Gill,[9] in 1944, reported the first adult case. Wise,[41] Waugh,[40] Trossero,[38] and Stobie [34] reported the only other adult cases. McLaughlin [24] reported the first case of splenosis producing a recurrence of congenital hemolytic icterus, and Stobie's case was the second. In Stobie's case, the patient continued to have symptoms after splenectomy, and during a Caesarean section, four years later, splenosis was found. It was noted that the capsule had been torn during the splenectomy.

Gill's case was also the first of subcutaneous implant of splenic tissue. His unusual case occurred in a man, aged 52, who had been shot in the left chest, at the level of the 9th and 10th ribs in the posterior axillary line. One year later repair of a diaphragmatic hernia and splenectomy were performed. At that time a subcutaneous mass in the region of the scar was noted. One year later, because of growth of this mass, it was removed. Microscopic section proved it to be splenic tissue. In Raper's case,[28] splenic tissue was found in the splenectomy scar.

The case reported by Shaw and Shafi [30] is of interest in that one implant was found in the pleural cavity. These authors believed that the implant had occurred through a rent in the diaphragm at the time of the automobile accident which necessitated the splenectomy.

In Bogg's [2] case and in one of Jarcho and Andersen's,[13] an autotransfusion of blood from the ruptured spleen was carried out. In the latter case autopsy was performed and only peritoneal implants were found.

An unusual case was reported by Eccles and Freer.[6] The patient was known to have malaria. In 1910 he had a splenectomy for ruptured spleen. All who were

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TABLE—*Summary of Literature*

Case No.	Author	Date	Sex	Age, Yr.	Age at Rupture, Yr.	Occasion	Time After Splenectomy	Location of Nodules	No.	Size of Implants
1	Albrecht [1]	1896	M	25	?	Autopsy	No history of trauma or splenectomy	Greater omentum; rectovesical pouch; domes of diaphragm	400	Hirshkorn to Hazelnut
2	Schilling [21]	1907	F	47	?	Autopsy	No history of trauma or splenectomy	Greater omentum; peritoneum of anterior abdominal wall; pelvis	42 (on greater omentum)	Pea to cherry
3	von Küttner [20]	1910	M	?	?	Autopsy	5 yr.	Throughout peritoneum	100	Pea to cherry
4	Faltin [7]	1911	M	9	3	Chronic appendicitis	6 yr.	On loops of large and small intestine	Numerous	Lentil to cherry
5	von Stubenrauch [29]	1912	M	?	?	Ileus	10 mo.	Greater omentum; transverse mesocolon; small intestine	Numerous	Hemp seed to pea
6	Ötman (quoted by von Stubenrauch)	1919	?	?	?	?	?	Throughout peritoneal cavity	Multiple	Not stated
7	Lee & Sheff [21]	1923	M	29	14	Ileus	15 yr.	Small intestine; mesentery	200-300	Pinhead to 1½ in. (3.7 cm.)
8	Kupperman [19]	1936	M	15	14	Postop. hernia	6 mo.	Small intestine; large intestine	100	Not stated
9	Shaw & Shafi [30]	1937	M	20	?	Autopsy	?	Abdominal wall; pleural cavity; liver; diaphragm; rectovesical pouch; greater omentum	82	0.2-2 cm.
10	Jarcho & Andersen [13]	1939	M	8	6	Autopsy (ileus)	18 mo.	Left dome diaphragm; liver; stomach; lesser omentum; transverse colon; right kidney; rectum; bladder	Several dozen	1-25 mm. in diameter
11	Jarcho & Andersen [13]	1939	M	20	12	Autopsy	8 yr.	Peritoneum; greater omentum; diaphragm; greater curvature stomach	80	1 mm.-2 cm. in diameter
12	Buchbinder & Lipkoff [2]	1939	F	28	8	Pelvic operation	20 yr.	Parietal peritoneum; greater omentum; ileum; sigmoid; ascending colon; liver; diaphragm	Numerous	1 mm.-2 cm. in diameter
13	Hamrick & Bush [10]	1940	M	13	9	Autopsy (tetanus)	39 mo.	Parietal peritoneum; pelvis; omentum; serosa of large and small intestine, diaphragm	Approximately 75	0.5-1 cm. in diameter
14	Krueger & Mast [15]	1942	M	16	11	Laparotomy for adhesions	5 yr.	Both surfaces of omentum	20-30	1-2 cm. in diameter

15	McLaughlin [24]	1942	M	(5 yr. difference) splenectomy for C. H. I.		Autopsy	5 yr.	Peritoneal cavity (patient still had congenital hemolytic icterus)	Many	1-3 cm. in diameter
16	Gill [9]	1944	M	54	52 yr. shot 53 yr., splenectomy	Subcutaneous mass, left chest	2 yr.	Chest wall, postaxillary line—level 9-10 ribs (abdomen not explored)	1	2 × 3 cm.
17	Boggs [2]	1945	?	14	11	Acute appendicitis	3 yr.	Over intestinal tract	25-30	1-2 cm. in diameter
18	Waugh [40]	1945	F	37	32	Hysterectomy (fibroids)	5 yr.	Small intestine; cecum	10 (seen)	Pinhead to pea
19	Bunch & Spivey [4]	1946	M	12	9	Appendicitis	3 yr.	Retroperitoneum; mesentery; greater omentum; pelvis	100	Pea to acorn
20	Stobie [34]	1947	F	29	25 (for C. H. I.; capsule torn)	Caesarean section	4 yr.	Pelvis; parietal peritoneum; uterus; omentum (patient still had C. H. I.)	Over 100	Pea to plum
21	Trossero [38]	1949	F	37	34	Hernia	3 yr.	Pelvic and peritoneum of abdominal wall	Numerous	Pinhead to lentil
22	Sampalo [29]	1950	F	19	9	Chronic appendicitis	10 yr.	Mesentery; anterior surface cecum; terminal ileum posterior peritoneum	Many	Not stated
23	Raper [25]	1951	M	About 30	?	Autopsy	?	Abdominal scar; parietal peritoneum; diaphragm; at foramen of Winslow; anterior stomach; ileum; omentum; pelvic peritoneum; mesentery	70	2 mm.-1 cm. in diameter
24	Wise [39]	1952	M	24	24	Intestinal obstruction	9 mo.	Omentum	10-20	Pinhead to 2 cm. in diameter
25	Storsteen & ReMine [35]	1952	M	22	16	Recurrent intestinal obstruction	5 yr.	Throughout peritoneum	300-400	1 mm.-2 cm. in diameter
26	Cohen	1951	M	30	Splenectomy, 8 yr. Purpura haemorrhagica	Mass in scar	22 yr.	In subcutaneous tissue of scar (abdomen not explored)	1	1.5 cm.in diameter

present stated it was completely removed. Eight years later he developed attacks of weariness and evening fever. In 1920 he underwent repair of a left rectus hernia. Well-formed, normal-appearing spleen was found in the usual position; there were many surrounding adhesions and a normal-looking pedicle, notch, color, and consistency. Schilling reported a case of Tedeschi's with primary atrophy of the main spleen and secondary hypertrophy of 50 splenules near the main splenic vessels, with 2 in the greater omentum. Jolly [14] reported a case of a 15-year-old girl who was operated on for acute appendicitis. Many round and oval nodules, measuring 0.1 to 0.5 cm. in diameter, were found. They were believed to be splenic tissue. Jolly was not able to ascertain the condition of the main spleen. There was no history of trauma or previous operation.

The last cases bring up the subject of accessory spleens. They have been reported in from 10 to 44%,* an incidence approximately equal to that of postoperative recurrence of thrombocytopenic purpura. However, autopsy material does not substantiate the theory that all recurrences are due to accessory spleens. The sites of occurrence, in order of frequency, are as follows: (1) splenic hilus, (2) pedicle of spleen, (3) retroperitoneal region around tail of pancreas, (4) omentum, especially at greater curvature of stomach, (5) splenocolic ligament, (6) mesentery of small and large intestine, (7) left adnexa, (8) rare sites (i. e., left scrotum). Most accessory spleens are found at one location, and when they are found at two places, one is at the hilus of the spleen. Accessory spleens are more commonly found in infancy.[34] Embryologically, the spleen begins at about the fifth week as a trilobated growth in the mesoderm of the dorsal mesogastrium between the mesonephric and the urogenital folds. Differentiation into one organ is completed by the 12th week. Haberer [31] has been quoted as the author of the term "accessory spleen." Such spleens are said to come from either cast-off lobulations of the main spleen or from anlage that did not form the main spleen. Accessory spleens differ very little, whether the main spleen is normal, enlarged, or removed. Therefore, the capacity of accessory spleens to enlarge is limited, and the possibility that they develop after splenectomy is unlikely. Accessory spleens have never been reported in congenital absence of the spleen, and they do not appear after splenectomy in animals in which they are normally absent.

The three main criteria by which to differentiate splenosis and accessory spleens [4] are as follows: 1. Accessory spleens are few and the nodules of splenosis many. 2. Accessory spleens occur near the splenopancreatic ligament in the supramesocolic region, and splenosis occurs all over the abdomen, and is especially submesocolic, as a result of gravity. 3. Microscopically, accessory spleens are like the main spleen, i. e., with normal hilus, capsule, and parenchyma. The nodules of splenosis have varying shapes, no hilus, and either partial or no capsule, and blood vessels are irregular in the parenchyma.

A review of the literature has revealed 25 cases (Table). I am reporting an unusual case, the third of a subcutaneous splenic implant.

REPORT OF CASE †

S. S. (U 84739), a 30-year-old white man, was admitted to Sinai Hospital, Baltimore, on June 28, 1951, with the chief complaint of a mass which he had noted three weeks previously

* References 5, 24, 36, and 37.

† Private case of Dr. Mark E. Gann, Senior Attending Surgeon, Sinai Hospital.

in the region of a left rectus scar. He had had a splenectomy for purpura hæmorrhagica in April, 1929. Physical examination was negative except for a nontender mass, 2 cm. in diameter, in the subcutaneous tissues just above the middle third of the abdominal scar. Routine laboratory tests, including bleeding time, coagulation time, and clot retraction determinations and tourniquet tests, were within normal limits. On June 29, 1951, the mass was removed from the subcutaneous tissues. It was bluish in color. The cut surface appeared fleshy. The postoperative course was uneventful.

Pathology Report.‡—Gross: Specimen consists of a portion of tissue from the abdomen. The portion of tissue consists of some yellow, fatty lobulated tissue and what appears to be a cystic structure, which measures 1.5 cm. in diameter. This cystic structure appears to be open and contains reddish-brown friable material.

Diagnosis.—Heterotopic splenic tissue showing the presence of an extensive histiocytic proliferation with fat deposits.

Much experimental work has been done on autotransplantation of splenic tissue. The first-known work is that of Giffini and Tizzoni,[8] who made multiple incisions into the spleen of a dog. Later, they found nodules of spleen-like tissue in the peritoneal cavity and on the omentum. They believed the nodules came from peritoneal rests. Von Stubbenrauch,[39] in 1919, reported the removal of the spleen in several dogs with seeding of the crushed splenic pulp throughout the peritoneal cavity. In three months splenic nodules were found in the peritoneal cavity. Von Stubenrauch had three theories to explain compensation for the loss of the spleen: (1) changes in the bone marrow and lymph nodes, (2) regeneration of the main mass of splenic tissue, and (3) formation in the peritoneal cavity of organs which have a structure like that of splenic tissue. These he termed splenoids.

Kreuter [17] did the same experiment in monkeys in 1919, as did Marine and Manley, in 1920,[23] and Putschar, in 1931.[27] These authors also proved the possibility of subcutaneous growth of splenic implants.

Shaw and Shafi [30] cited Guerrini's case of a dog examined months after severe abdominal trauma. A large hematoma of the spleen and numerous nodules of splenic tissue were found in the peritoneal cavity. He thought they were hypertrophied accessory spleens.

Perla [26] followed the microscopic growth of the splenic inferior pole of a rat autografted to the abdominal wall. Ninety per cent of this tissue grew, even though a part of the main spleen remained. It was found that the transplanted tissue underwent rapid degeneration within the first 24 hours. A thin zone of viable reticular cells survived. There was little inflammatory reaction around the transplant. By the third day, there was marked proliferation of the reticular cells at the outer zone, and streams of cells were seen penetrating the necrotic center of the transplant. In some instances, the entire transplant was replaced by reticular cells which formed the pattern of a sinus organ. By the third or fourth day, lymphocytes appeared regularly in clusters, and apparently all stages of lymphoid-cell formation were observed. By the sixth day, the outer two-thirds of the transplant was replaced by reticular elements arranged in an intricate mesh as in the adult spleen, with sinus formation and ill-defined clusters of lymphocytes. Complete regeneration of large transplants occurred from the 12th to the 21st day, and the morphologic structure of adult splenic tissue was apparent, with well-developed capsule and trabeculae. Perla believed

‡ Reported by Tobias Weinberg, M.D., Chief of Department of Pathology, Sinai Hospital.

that the reticular cell retained its potentiality for differentiation and may be the precursor of the structural elements of the spleen. Manley and Marine [22] believed regeneration in splenic autotransplantation involved all structures in normal proportion in their rabbit experiments. In later experiments,[23] they felt there was decrease in the amount of growth as one passed from youngest to oldest and no marked growth if the spleen was not removed. They believed splenic function may be undertaken by other tissues (such as lymph nodes and bone marrow) in the adult.

The entire spleens of rats have been transferred from the abdomen of one to that of another, with some survival.[16] Homotransplants showed failure after a few months of growth,§ except when the transplant was taken from an embryo rabbit over 17 days old to the omentum of an adult rabbit.[12] Syngenesiotransplantation ‖ was also a failure.[33] Spleen transplanted to the thyroid and renal regions failed to grow.[15] Williams,[42] by a unique technique, studied splenic autograft growth. He made a microscopic chamber in a rabbit's ear with tantalum mesh and mica and placed a splenic autograft there. He saw a splenic macrophage ingest eight red blood cells and destroy them in three hours. Epinephrine (Adrenalin) stopped the arterial flow. Grafts of Malphigian bodies or capsule did not survive. Intravascular fragmentation of protoplasmic masses was also observed, a process which may represent platelet formation.

Perla [25] did further experiments which suggested that a spleen-stimulating factor was present in the anterior hypophysis. It was present in the extract containing growth and gonadotropic factors.

The entire spleen has been successfully transplanted to the abdominal wall [11] supposedly to decrease portal hypertension by forming venous collaterals.

The reason so few cases of splenosis have been reported can be understood from the following observations. Such extensive trauma to the normal spleen as to rupture it and require splenectomy is rare.[18] A very high mortality [40] is associated with splenic rupture, and the occasion to reopen the peritoneal cavity after splenectomy is slight. The time between splenectomy and the finding of splenosis has varied from 6 months to 20 years. It is of interest that splenosis has not been described after splenectomy for spontaneous rupture of the diseased, enlarged spleen.

Transplanted splenic nodules have been found to carry out normal splenic function. The case of Shaw and Shafi showed miliary tubercles and erythrophages in the splenic nodules. Gill's case had recurrent malaria after splenectomy. The splenic nodule was probably the source of the parasites. Boggs [2] also believed the implants could carry out normal splenic hematopoietic function. Many implants contain pigment, probably derived from destroyed red blood cells.

Stobie has suggested that all the blood be removed from the abdominal cavity after splenectomy to prevent splenosis.

The average case of splenosis could be described as occurring in an adult operated upon for an abdominal condition or autopsied. The patient had had a splenectomy for traumatic rupture of the spleen in his youth. Many 1 mm.- to 3 cm.-sized, dark-blue nodules, sessile or pedunculated, are found throughout the peritoneal cavity. Microscopic section reveals normal appearing splenic tissue, but no normal capsule or hilus.

§ References 15, 22, 23, 32, 33, and 43.

‖ Transplantation in blood relations.

SUMMARY

A review of the history and modern literature of splenosis (autotransplantation of splenic tissue) is given. The embryology of the spleen and the subject of accessory spleens are described.

The experimental work on splenic transplantation is reviewed.

A case of a subcutaneous splenic implant is reported.

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CLINICAL AND SOCIAL PROBLEMS ASSOCIATED WITH FAMILIAL INTESTINAL POLYPOSIS

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FAMILIAL intestinal polyposis is a rare hereditary disease characterized by the growth of very many adenomatous polyps from the rectal and colonic mucosa. The polyposis (Fig. 1) generally develops in adolescence or early adult life, though more rarely it may occur in the first decade or after middle age. The disease appears to be inherited as a heterozygous, dominant Mendelian characteristic; thus, only an affected parent, either male or female, can transmit the disease, and then only to half the children.

Colonic polyposis is probably the most clearly defined precancerous disease known to medical practice today. Dr. Cuthbert Dukes,* who has followed the course of this disease at St. Mark's Hospital for many years, has recently (1952) reviewed 156 cases and shown convincingly that malignancy develops in one or more polyps with grim punctuality 10 to 15 years after the first symptoms of polyposis and that the expectation of life of an affected person is only 41.6 years. The rate of growth of the polypi and their tendency to undergo malignant change vary from family to family, but in general it appears that the earlier the disease occurs the more rapid its course, while after middle age the polyps develop more slowly.

Familial polyposis of the colon should be differentiated from congenital polyposis affecting the whole gastrointestinal tract, a disease which is accompanied by skin pigmentation.[3] The obvious skin marking and the early obstructive symptoms from the benign polyps of the small intestine soon bring such patients for medical advice, whereas the symptoms of polyposis of the large bowel may be relatively trivial until malignancy supervenes. Isolated polyps in the rectum are not uncommon and should not be confused with colonic polyposis, in which the polyps are much more numerous and widespread. If an adult is seen to have a few polyps only on sigmoidoscopic and x-ray examination, the case should not immediately be diagnosed as one of colonic polyposis.

It is not yet understood how the disease originates in a family. J. P. Lockhart-Mummery † postulated that the polyposis arises as a mutation and that it is inherited thereafter. A minority of patients with colonic polyposis do not appear to have inherited the disease, as their parents and brothers and sisters are unaffected. These isolated cases have not yet been followed long enough at St. Mark's Hospital to determine whether they will transmit the disease to their children as the original

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* References 1 and 2.

† References 4 and 5.

case from which the familial disease stems, or whether they are suffering from a nontransmittable form of the disease which is otherwise similar to familial polyposis. In the two families here reported the disease was already established in the earliest generation to which the family could be traced with accuracy.

The purpose of this paper is to discuss the various problems that arise during the investigation of families affected by familial polyposis and to report two families which I assisted in investigating during the tenure of a Research Fellowship at St. Mark's Hospital, London. At St. Mark's Hospital, 55 polyposis families have now been investigated and the family pedigrees prepared. The families include 1,036 members, using the word "member" to describe polyposis patients, their brothers and sisters, and the direct descendants of these persons. Of these 1,036 members, no less than 208 are known to have suffered from polyposis, and 150 of these have already developed intestinal cancer.‡

Fig. 1.—Polyposis involving the whole colon; total colectomy specimen from Member IV, 2 of the first family.

THE FIRST FAMILY

The pedigree of this family is shown in Figure 2; Table 1 gives a summary of the affected members.

‡ Dukes, C. E.: Personal communication to the author, 1954.

FIG. 2

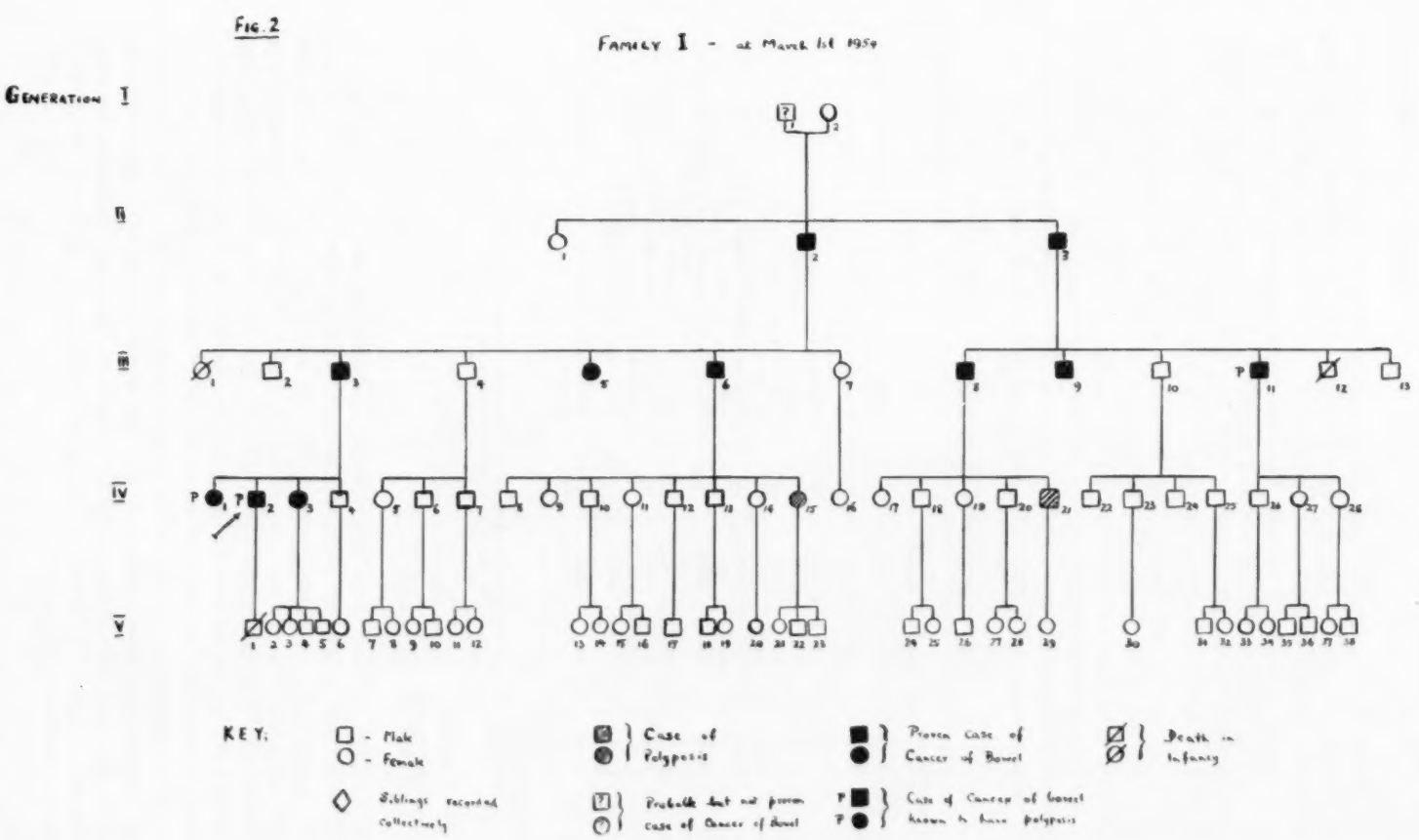


Fig. 2.—Family I, March 1, 1954.

The first patient in this family was a machine operator, aged 40 (marked in the pedigree as IV, 2). He was admitted to hospital in November, 1952, with advanced polyposis and an early carcinoma of rectum. In his family there had been 10 cases of cancer of the large bowel within three generations, but the familial character of the disease had not been recognized. Of these 10 cases, the majority had had only palliative treatment, and there was only one survivor (III, 11), who had had an excision of rectum and pelvic colon nine years earlier.

At the time of the investigation, there were 4 living members of the third generation and 21 of the fourth. The members of Generation IV were all traced, and all offered examination except one; this member (IV, 16) was not approached, as she had not been brought up as a member of the family and was unaware of her true parentage; it was thought that it was unlikely that she could have inherited the disease, as her mother was alive and symptom-free at the age of 60. Of these

TABLE 1.—*Summary of Affected Members of First Family*

Generation; No.; Sex	Date of Birth	Age at Death	Cancer	Comments
I 1 M	1827	63	?	Death certificate states "Visceral disease with peritonitis of 5-mo. duration"
II 2 M	1853	43	+	Carcinoma of rectum
3 M	1857	53	+	Carcinoma of rectum
III 3 M	1882	46	+	Carcinoma of descending colon
4 M	1883	35	..	Killed in 1914-1918 war
5 F	1886	32	+	Carcinoma of rectum
6 M	1890	43	+	Carcinoma of sigmoid colon
8 M	1881	63	+	Hepatic metastases with history of diarrhea
9 M	1885	29	+	Carcinoma of rectum
11 M	1890	Alive	+	Polyposis and carcinoma of rectum; excision of rectum and sigmoid at age 54
IV 1 F	1911	37	+	Carcinoma of rectum
2* M	1912	40	+	Polyposis and carcinoma of rectum
3 F	1914	27	+	"Abdominal carcinoma"—death certificate
15† F	1926	Alive	Polyposis only	Early case—no symptoms
21† M	1923	Alive	Polyposis only	Total colectomy and ileorectal anastomosis

Investigation:
Generation IV: IV 8, 9, 17, and 24 had died of other causes before 1953.
IV 4, 13, 14, and 18 have refused examination.
IV 23 was found to have three simple rectal polyps.
Generation V: V 2 only has been examined, and is unaffected. All members of Generation V are under 19 years of age.

* Presenting case.
† Case discovered during investigation.

20 members, 16 have been sigmoidoscoped, confirming that the descendants of III, 4 and III, 10 are free of the disease and finding two new cases (IV, 15 and 21), both children of affected parents. The children of III, 11 are free of the disease at present, though they are still young, being 36, 32, and 21 years of age respectively. One of the new cases (IV, 21) had had symptoms for three years but had not sought medical advice, as he thought that the disease was incurable, since no treatment had been offered to his father before his death.

The average age at death of the affected members was 41.9 years. The duration of symptoms prior to the finding of carcinoma appears to be shorter than in other families reported, no patient being noted to have had symptoms for more than three years. The hereditary pattern of the disease in the family is typical of familial intestinal polyposis.

THE SECOND FAMILY

The pedigree of this family is shown in Figure 3; Table 2 gives a summary of the affected members.

In 1935, Mr. W. B. Gabriel treated Member II, 11 at St. Mark's Hospital and subsequently investigated her children; unfortunately, the cooperation of this part of the family was never freely given, mainly because the father believed that all

TABLE 2.—*Summary of Affected Members of Second Family*

Generation; No.; Sex	Date of Birth	Age at Death	Cancer	Comments
I 2 F	1862	42	+	Death certificate does not state organ involved
II 2 F	1880	60	+	Carcinoma of rectum
3 F	1882	49	?	Death from diabetes; symptoms of polyposis prior to death
5 F	1885	19	?	Death certificate states "sarcoma of spleen"; symptoms of colonic cancer
8 F	1891	44	+	Polyposis and carcinoma of transverse colon
9 F	1893	30	?	Died of pneumonia
11 F	1898	49	+	Polyposis and carcinoma of colon
III 5 F	1905	33	+	Death certificate states "fibrosarcoma of abdominal wall"; probable metastasis in laparotomy scar
6 F	1909	30	+	Carcinoma of rectum
9* M	1903	Alive	+	Polyposis and carcinoma of rectum; excision of large bowel in 1952
10† M	1904	Alive	Polyposis only	Advanced polyposis; patient refuses operation
12 M	1909	38	+	Polyposis and carcinoma of sigmoid colon
19† M	1923	Alive	Polyposis only	Advanced case; under investigation prior to treatment
20 M	1924	1½	+	Hepatoblastoma
24† M	1921	Alive	Polyposis only	Early case
29‡ M	1920	30	+	Polyposis and carcinoma of rectum; operation refused
31‡ F	1924	Alive	Polyposis only	Defaulted from follow-up after 1941
IV 4† F	1929	Alive	Polyposis only	Early case
15† M	1930	Alive	Polyposis only	Total colectomy, 1952
20† F	1939	Alive	Polyposis only	Early case
27† M	1934	Alive	Polyposis only	Total colectomy in 1951

Investigation:

Generation II: II 6, 7, and 10 were alive in 1953; they were all symptom-free and were not examined.

Generation III: III 2, 4, 7, 21, 22, and 33 had died of other causes before 1951.
III 17 has not yet been traced.
III 8, 11, 16, 23, and 32 have not yet been examined; nor have the children of II 7 and 10.

Generation IV: IV 30 had been killed in an air raid; all the other members were alive.
IV 5 has not yet been traced.
IV 11, 17, 18, 22, 23, and 24 have not yet been examined.
IV 32-43 are all under the age of 12 and have not been examined.

All members of Generation V are under 12 years of age.

Note: The diagnosis in every case in both families has been confirmed from death certificates or hospital records.

* Presenting case, 1951.

† Cases found in 1951 and 1953 investigations.

‡ Case discovered before 1951.

treatment was meddlesome. They would not communicate with their relatives or give their addresses; the father carried his opposition to the extent of preventing his son from having treatment; subsequently the son developed a rectal cancer and died at the age of 30.

FIG. 3

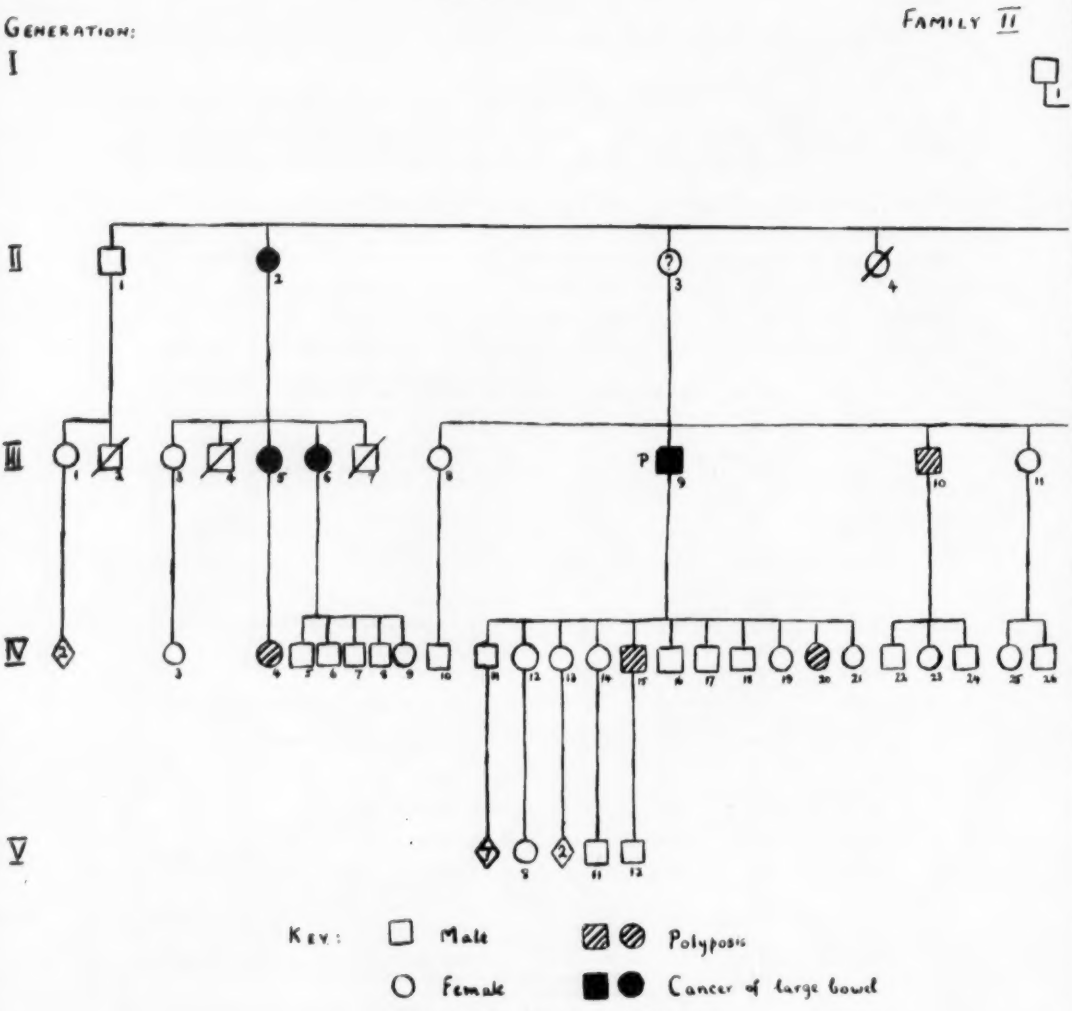
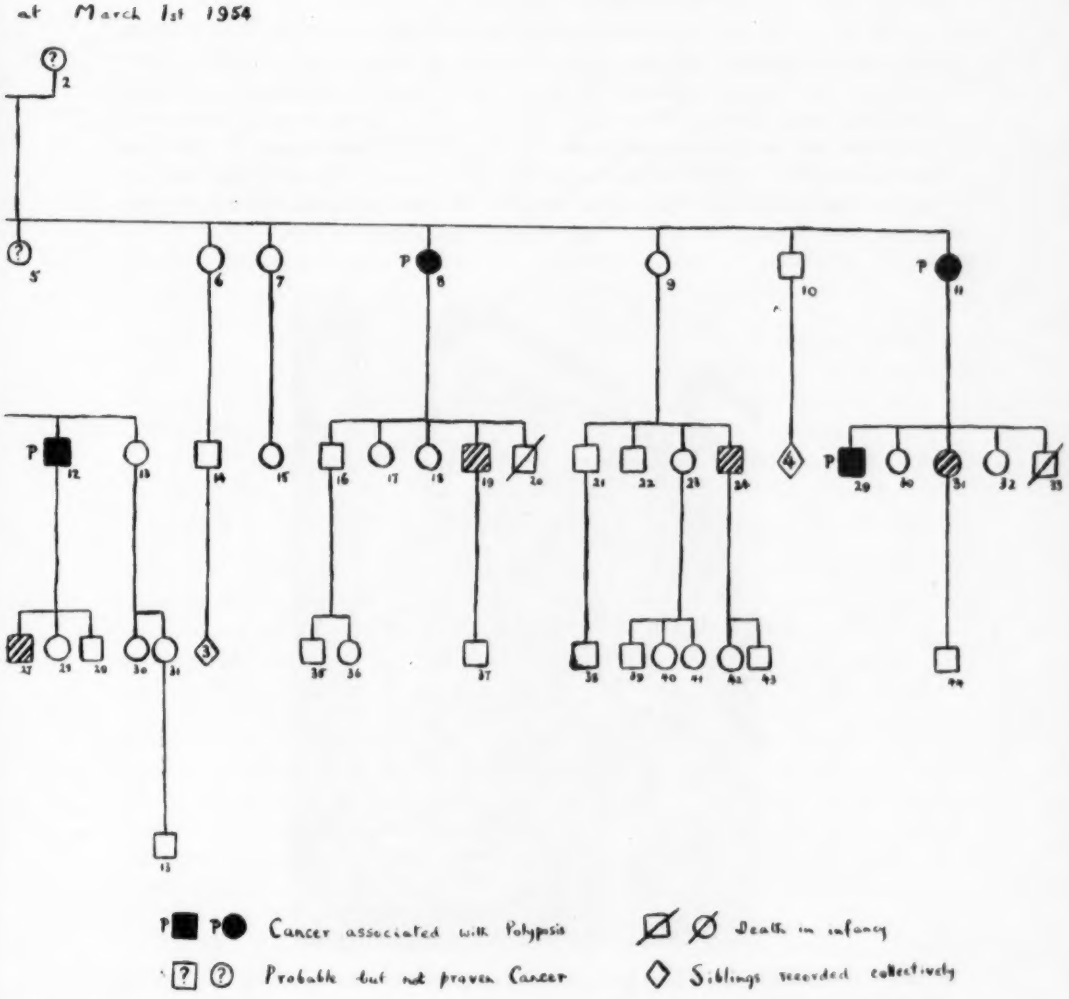


Fig. 3.—Family II, March 1, 1954.

In 1951, Mr. H. R. Thompson was asked by Mr. R. Parkinson, at East Ham Memorial Hospital, to examine and advise in the treatment of a patient with polyposis and two rectal carcinomata. Only when this patient's (III, 9) family tree was constructed was it found that he was a nephew of II, 11. At this time Mr. H. R. Thompson traced and examined the majority of the patient's near relatives. During the autumn of 1953, a further investigation of the family was carried out and an attempt made to trace the rest of the relatives and to encourage them to be examined.

The typical hereditary pattern of the disease is not so clearly shown in this family as in the first; this is due to the early death of several members of the



family from other diseases, although they have transmitted the disease to their children. These early deaths have also led to the family becoming split into small groups, with little knowledge of one another. This factor has greatly increased the difficulty of tracing all members of the family, and it has prevented the cooperative members of the family from having their usual helpful influence on those who are unwilling to be examined. However, despite this, all the children of affected members except two have been traced and the majority of them examined.

A full key to the two family trees and the medical records of the affected members are filed in the Polyposis Register of the Research Department of St. Mark's Hospital, where they are available for reference.

PROBLEM OF THE AFFECTED INDIVIDUAL

The growth of the intestinal polyps is generally far advanced before a patient seeks medical attention because of his symptoms. The incidence of cancer in these persons is distressingly high; C. W. Mayo,[6] in a series of 45 patients undergoing colectomy, found that only 6 were free from cancer and that in many cases there was more than one focus of malignant disease. In nearly all cases, a careful histological search throughout the colon and rectum will show areas of great epithelial hyperplasia, which, although there is no invasion or gross irregularity of cell architecture, can be but a short step from frank carcinoma (Fig. 4).

Fig. 4.—Epithelial hyperplasia in a colonic polyp; × 190. Specimen from Member IV, 21 of the first family.

Diarrhea is the earliest symptom of the disease and at the outset may be very slight, amounting to little more than a soft consistency of the feces. The insidious progression of this symptom is not noticed by the patient, who comes to think that it is normal for him to have more frequent bowel actions than his fellows. Late in the disease, the diarrhea increases, interfering with the patient's daily life, while hemorrhage and mucous discharge from the polyps give rise to symptoms which cannot be disregarded.

The presence of malignancy in a case of intestinal polyposis calls for early and radical treatment, and in advanced cases of polyposis, without clinical carcinoma, treatment cannot be long delayed. On the other hand, the early case found during

an investigation of an affected family raises not only the problem of what treatment to advise but when the treatment should be undertaken.

At present, the only treatment that will certainly prevent the seemingly inevitable malignant change in the polyps is the excision of all the affected bowel. To excise the whole colon and rectum for a condition not yet malignant, and to leave a young, and otherwise healthy, patient with a permanent ileostomy, is a drastic undertaking. It seems reasonable to take advantage of the fact that in some cases the rectum and lower sigmoid can be cleared of polyps by fulguration through a sigmoidoscope and to anastomose the terminal ileum, after colectomy, with the lower large bowel so cleared. After this treatment, the patient will have to submit to sigmoidoscopic examination at regular intervals, so that any polyps that continue to form in the large bowel remnant can be fulgurated. It is not yet certain that fulguration of all polyps as they form will prevent the development of rectal cancer, as it is possible for malignant change to occur in a minute polyp; nevertheless, it appears justifiable to take this risk to preserve normal bowel function in a young person.

The clearing of the rectal polyps by fulguration is generally best done before the colectomy, as afterwards the ileal content tends to obscure the rectal mucosa. The anastomosis between the ileum and the remaining large bowel must be within reach of a sigmoidoscope; the higher the anastomosis, the easier it is to perform and the more normal the postoperative bowel function is likely to be. These advantages of the ileosigmoid and high ileorectal anastomosis over a lower ileorectal anastomosis are offset by the larger area of mucosa left in situ from which new tumors may arise and the greater difficulty that their fulguration will present. In more severe cases the rectal polyps may be so numerous that fulguration of all of them will leave the rectum so scarred or stenosed that its function will be impaired. In these cases the only alternative to excision of the rectum and establishment of a terminal ileostomy is to remove the whole rectal mucosa, leaving the muscular wall of the rectum and passing the terminal ileum through this muscular tube to anastomose it to the anal mucosa.§ This operation has the advantage of removing all the tumor-bearing mucosa, but it has not yet been fully established that this anal ileostomy is controlled by the preserved sphincters adequately enough for the patient to lead a normal life.[9]

Operative treatment of this disease still carries a definite mortality. If it were not for this fact, it would be logical to advise prophylactic colectomy for all patients as soon as they are found to be affected and it is certain that the disease is progressing. Colectomy for polyposis in adolescence has many advantages; it is undertaken before the patient's adult career has started, and when his physical fitness is greatest and his social commitments least. The risk of malignant change increases with every year of adult life that treatment is postponed. There is also the risk that certain patients will not tolerate prolonged observation before treatment and may default at the crucial time. Once malignancy develops, the chance of cure decreases rapidly; it is imperative, therefore, that treatment be carried out while the disease is still in its precancerous stage. At present the age at which malignancy will occur in any one case cannot be accurately assessed, although the age incidence of malignancy in the family, the duration and severity of the symptoms, and the degree of

§ References 7 and 8.

polyposis give some indication of the age at which this change may be expected. It must be remembered that a barium enema will not show early malignant change in a polyp and that the polyposis in the colon may be more advanced than in the portion of the rectosigmoid visible through a sigmoidoscope. Each case must be judged on its own merits, and in timing the operation, all these factors must be evaluated. It is unwise to delay operation once the risk of malignant change has become greater than the risk of treatment.

The good will of the other members of the family is likely to depend on the handling of the first affected member. The cooperation of the other members of the family and their willingness to take medical advice are greatly increased if a relative has been successfully treated, whereas the death of a relative after operative treatment or while under observation will confirm them in a fatalistic and defeatist attitude towards the disease.

PROBLEMS ARISING DURING INVESTIGATION OF AN AFFECTED FAMILY

One would expect, in a disease of this type, that the members of the affected family would be very willing to take medical advice and cooperate in being examined, as the majority of them must be aware that in ignoring this advice they are running the risk of developing a lethal disease at a relatively early age. Unfortunately, this is not always the case, and it is often more difficult to persuade a member to be examined than to trace them after they have lost touch with their family. The two main reasons for this are the fatalistic attitude which the family members tend to adopt toward the disease, sometimes amounting to a denial that the disease exists or that it can affect them personally, and their fear of treatment, which they associate with colostomies and failure to cure their older relatives.

Ideally, all members of the family should be traced, and those who may possibly inherit the disease should be examined at intervals until they are past the age when the disease is likely to develop. The wholehearted confidence and good will of the family is needed to achieve this ideal; without it, the good intentions of the enthusiastic doctor are likely to be thwarted by obstructive tactics, if not by open opposition.

The tracing of the various members of the family may involve the investigator in some interesting detective work. The early death of a parent may result in the break-up of the home; the children may be officially or unofficially adopted, or the surviving parent may remarry, losing touch with the affected parent's family. The surviving parent may even become hostile to the former in-laws, feeling that they have been responsible for the disease. Faced with these circumstances, it may happen that seemingly trivial pieces of information may provide a clue to the whereabouts of a relative or his descendants. For instance, in the second family, shortly after one woman had died of carcinoma of the colon, her husband committed suicide; their children were cared for by friends, but soon left to make their own way in the world. The only information that Mr. H. R. Thompson had about them was that the two sons had taken up professional boxing in the East End of London. All inquiries of professional and amateur boxing boards were fruitless until it was discovered that a professional boxer frequently fights under another name; the boys were finally found using their maternal grandfather's name. Two other groups in this family were brought up in orphanages and became widely scattered when they

had grown up; two members remain untraced—one was adopted unofficially as an infant and the other deserted during his military service.

The fear that some social stigma, especially illegitimacy, may be brought to light by the investigation sometimes causes a family to be reticent. Illegitimacy is not an uncommon finding in these families, apparently due to the early loss of a parent and the breaking up of the home. Sooner or later, when the investigator has gained the confidence of the family, there may be a number of surprising disclosures which often explain the earlier lack of cooperation. If children have been adopted, it is important that they are traced, though they, or their foster-parents, need be approached only if there is a definite risk of the child having inherited the disease. It seems fairer not to approach them while the children are still young, but to do so when the children are old enough to be examined and are able to make up their own minds about the matter. If they are not traced and later develop the disease, its familial nature will not be obvious, and it may appear to be an isolated case.

It has been suggested that environment may play a part in the etiology or modify the course of the disease, but it must be remembered that the ill health and early death of an affected father will leave his children in poorer circumstances than the rest of the family, so that his children inherit both the disease and the poorer environment. In these two families, the difference in social standing of the affected and the unaffected branches was quite marked and tended to produce a cleavage in the family as a whole; also, the members of the affected branches were less well educated, and so more distrustful of the investigation and less ready to grasp the reason for it and the need for their own examination.

Once a member of the family is traced, contact is best made by a personal visit to their home. Letters of inquiry are often resented and produce far less information; if a visit is impossible, then the letter should be personal and informal and not set out as a questionnaire. During the visit, every effort should be made to put the member at his ease, as the nature of the investigation often causes him alarm. Patience and tact are needed to overcome his natural reticence and fear. Personal questions should not be asked at first, but inquiries made about the past history of the family and the more distant relatives, gradually turning the conversation to the near relatives. If possible, the conversation should be so directed that the member is brought to see the need for an examination and asks about it himself. If he does not do this, the question should not be pressed at the first visit, especially if he is likely to be affected, and so probably more fearful. The general practitioner is often in the best position to convince the member of the need for an examination and to change any fatalistic attitude toward the disease; he can also encourage an affected patient to attend regularly, both before and after operation.

A member's cooperation is generally obtained more easily by reassuring him than by frightening him. Family gossip often exaggerates the incidence of the disease, so that some members come to think that the whole family is doomed to develop cancer. It is reassuring to explain that only half the children of an affected parent are likely to develop the disease, so that each one has as good a chance of being free as of being affected. Further, if they are not affected and remain so throughout life, there does not seem to be any chance of their transmitting the disease to their children. Other common misconceptions are that it is cancer that is inherited, and therefore that the disease is incurable, and that treatment is purely experimental

and often "spreads the cancer." It should be stressed to them that polyposis is not malignant in its initial stages and that much can be done by timely treatment. The question of treatment is best not raised too early, as the mention of operations may increase the agitation that has already been aroused by the inquiries; the fact that treatment nowadays can leave the patient quite normal, without the need for an artificial bowel opening, is all that need be mentioned.

The investigation of families of this size is never completed; the family grows and changes from year to year. It may be difficult to maintain contact with affected members so that their children can be examined at the right moment. Dr. Cuthbert Dukes, in following up the families under surveillance at St. Mark's Hospital, has devised a system of "collaborators." || These collaborators are members of the various branches of the family; they may be old or young, male or female, affected or unaffected; the one quality for which they are chosen is their "tribal" outlook, their knowledge and interest in family affairs. On their various birthdays they receive a letter with a stamped addressed envelope enclosed—they seldom fail to reply, giving all the recent family news.

SUMMARY

Two large families affected with intestinal polyposis are reported. The problems that arise in treating and investigating this disease are discussed. The major problem is the treatment of the affected member. At present, radical surgery offers the only hope of a permanent cure; the age at which this treatment should be carried out is still controversial and is discussed.

My experience with these two families has convinced me that in accepting the responsibility of treating an affected member, the surgeon should also take the responsibility of investigating the whole family. Only if active investigations of these families are carried out will the high incidence of malignant change before treatment be lowered.

Mr. H. E. Lockhart-Mummery and Mr. G. G. C. Taylor examined many of the patients of the first family. Mr. W. B. Gabriel and Mr. H. R. Thompson allowed me access to the records of the second family, who were under their care. This family had already been thoroughly investigated by Mr. H. R. Thompson, and all I have done is to bring that investigation up to date.

A grant from the British Empire Cancer Campaign facilitated these investigations.

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INTRALOBAR PULMONARY SEQUESTRATION

Report of Three Cases, with Two Additional Cases of Agenesis of the Right Upper and Middle Lobes in Combination with Anomalous Systemic Vessels

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INTRALOBAR pulmonary sequestration was described by Pryce as an anomalous artery running from the aorta in the vicinity of the diaphragm to the lung and a congenital bronchopulmonary sequestration or ectopia in the area of the lung served by the anomalous vessel.[1] He classified the arterial anomaly into three types, in which the abnormal artery supplied only normal lung tissue, sequestrated lung alone, or both normal and sequestrated lung. The sequestration consists of bronchogenic cystic disease, which is described by Strode as cysts having walls composed of bronchial elements, viz., cartilage, elastic tissue, smooth muscle, and mucous glands.[2] The lining consists of cuboidal or columnar epithelium, which is frequently ciliated. The contents of these cysts may be fluid, pus, blood, or air alone or in combination with the named fluid elements. The sequestrated portion usually has no communication with the normal bronchi and is thus not demonstrated in a direct manner by bronchography.

This condition should be distinguished from extralobar sequestration or lower accessory lung. Here a separate portion of lung is found, commonly in the inferior portions of the thoracic cavity, with a hilus which may be attached to the parietes, esophagus, or diaphragm. Its bronchial system does not communicate with the normal bronchi, and the venous drainage is to a convenient system, most frequently that of the gastrointestinal system or azygos system. These lobes may be found in the supradiaphragmatic or the infradiaphragmatic position.

Prior to the work of Pryce there had been several descriptions of anomalies of a similar nature. Haight,* McCotter,[4] Batts,[5] and others described the vessel anomaly. Boyd [6] and Hertzog [7] described cases in which the anomalies were combined. The majority of the authors writing on this subject have given their support to the idea that the etiology of this disorder lies in the persistence and traction effect of a lower accessory pulmonary artery arising from the primitive splanchnic plexus and "capturing" an end-bud of normally developing pulmonary tissue.

We are presenting three typical cases of this disorder. In addition, we are presenting two cases with anomalous vessels from the aorta in combination with agenesis of the right upper and middle lobes.

From the Department of Surgery, the University of Chicago.

This work was supported by the Douglas Smith Foundation for Medical Research of the University of Chicago.

* Haight, C., in discussion on Brown and Brock.[3]

DIAGNOSIS

Routine roentgenographic examination of the chest may disclose a lesion in the lower lobes, especially in the posteromesial portion, which has been silent. A commoner situation is that in which the sequestrated portion becomes infected. The infection may result from juxtaposition to and direct extension from normal lung parenchyma which has become infected. The ectopic portion retains the infection, primarily as a result of its lack of an orifice through which to discharge the purulent contents.

A chronic pulmonary infection of this type most frequently presents itself with a cough as the dominant symptom. Productive cough, respiratory embarrassment, hemoptysis, and asthma may also be presenting complaints. Clubbing of the fingers may be found, as in one of our cases (Case 2) and in McDowell's.[8]

Although the condition may be suspected, exact preoperative diagnosis is not often possible. This lesion most frequently presents an appearance on x-ray of a mass or a fluid-filled cyst in the lower posteromesial portion of the lung. The appearance itself is not diagnostic. Bronchoscopy and bronchography will sometimes aid in the diagnosis and localization. None of our patients had positive tuberculin tests, but several cases in the literature proved to have a tuberculous infection in the sequestrated portion.†

The side of involvement has been studied and discussed by several authors. Bruwer's series of intralobar ectopia indicated left-sided dominance.[10] In our series, two of the cases of sequestration and both cases of agenesis of part of the lung were encountered on the right side. There is some evidence that the supradiaphragmatic vessels supply the left side most commonly, whereas those arteries which perforate the diaphragm are associated with right lung ectopia.‡

TREATMENT

Surgical extirpation of the sequestrated segment or of the lobe containing the segment is the treatment of choice in this disease. Consideration of the presence of the anomalous vessel will help to avoid instances such as those fatal cases of Douglass [12] and Harris and Lewis,[13] in which the anomalous vessel was interrupted and the patient died of exsanguination.

DEVELOPMENT

Cole and associates wrote in 1951 reporting six cases of intralobar pulmonary sequestration.[14] They reviewed the theories of etiology and concluded that our knowledge of teratology was insufficient to explain the basic defect productive of this disorder. The present-day theories explaining this disease are five in number:

1. Portion of lung "captured" by anomalous artery§
2. Reduplication from digestive tract [15]
3. Deepening of normal or abnormal intralobar fissures [15]
4. Amputation by pleuroperitoneal iter to explain cases of lower accessory lung in abdomen [15]
5. Embryonic adhesions between lung bud and adjacent tissue [15]

† References 6 and 9.

‡ References 10, 11, and 16.

§ References 1 and 15.

The last three theories are self-explanatory. The theory presented by Pryce can be summarized as assuming that the anomalous vessel is the prior abnormality, the traction of which (during the 10 to 14 mm. stage of embryonic development) on a "captured" bulbous tip of the developing bronchial tree produces the diseased state.[1] He goes on to explain how the anomalous artery from the dorsal aorta may capture a portion or all of the respiratory anlage at an earlier embryonic age and produce all manner of dislocation, from lower accessory lobes to agenesis.

Many of the writers on this subject, including Ripstein,[18] Boyd,[6] and Bruwer and associates [10] support this theory. Authors, such as Tosatti, consider the total situation to consist of the persistence of an anomalous vessel together with the congenitally cystic lung.[9]

Eppinger,[16] Baar and d'Abreu,[17] and others credit intralobar ectopia to accessory respiratory anlage developing from the primitive foregut. Eppinger was the first who attempted to explain lower accessory lobes on the basis of accessory respiratory anlage. Baar and d'Abreu have written the most recent paper supporting this theory and explaining the anomaly as a result of interference with the metabolic gradients involved in embryonic development, producing failure of resorption of accessory buds of the foregut, with dislocation of these buds and their development into anomalous residua, such as lower accessory lobes.[17]

PRESENTATION OF CASES

These five patients were all hospitalized in Bob Roberts Memorial Hospital, University of Chicago Clinics, and were operated on by one of us (W. E. A.).

CASE 1.—M. R., a 3¼-year-old white girl, was in good health until the age of 23 months, when she developed acute tonsillitis, with temperature of 39.5 C. (103.1 F.). Two weeks later she developed what was thought to be a pleural effusion, was hospitalized, and 250 cc. of thick brown sterile fluid was aspirated from the left chest. During this interval she received penicillin. She was then well for 11 months, at the end of which time she developed a respiratory illness, complicated by what was thought to be another pleural effusion, which was again treated with aspiration and antibiotics. She was then well for 3 months, when, after a third respiratory infection, she was hospitalized at Bob Roberts Memorial Hospital. On admission the patient appeared to be acutely ill; she had a temperature of 38.4 C. (101.1 F.) and a deep, raspy cough. Tuberculin skin tests were negative down to 1:100 dilution. The chest x-ray revealed a multilocular cyst of the left lower lobe, with fluid levels. After treatment with sulfadiazine and penicillin, the patient underwent exploration of her left chest, on April 15, 1953. The left lower lobe was atelectatic and infiltrated, and it was noted that a large artery ran from the aorta in the region of the diaphragm to the posterior basal region of the left lower lobe. A left lower lobectomy was carried out. There were two small, relatively normal, areas in the lung, one in the superior segment and one in the anterior medial segment. The remainder of the lobe was grossly infiltrated. The main-stem bronchus ended blindly after a 2 cm. course. The main substance of the lobe was made up of a thick-walled, multiloculated cavity, 6 cm. in diameter, which communicated with several smaller cavities. This cavity was filled with thick purulent exudate. Microscopically the cysts were lined by pseudostratified and usually ciliated respiratory epithelium. There were a few normal air-containing alveoli. There was considerable, severe, chronic bronchopneumonitis in the remainder of the lobe. In the region of the abnormal artery there were small accompanying veins, numerous large lymphatic vessels, nerves, and several lymph nodes. The lung tissue in this area was notably hypoplastic. The postoperative course was relatively uneventful.

Comment.—This case is considered one of intralobar pulmonary sequestration demonstrating the recurrence of infection as a characteristic of the disease.

CASE 2.—A. N., a 27-month-old Japanese girl, was well until the age of 13 months, when she developed pneumonia. After this, she had a persistent, nonproductive cough, but no other signs of

illness until four days prior to her admission here. At that time, she developed a cough productive of large amounts of thick foul sputum. That evening she became febrile and was x-rayed. She was referred to Bob Roberts Memorial Hospital with a diagnosis of lung abscess. On admission she was acutely ill, with a temperature of 39.0 C. (102.2 F.). She had a loose cough, productive of large amounts of foul sputum. There was mild clubbing of the fingers. X-rays of the chest revealed cystic lesions in the right lower lung field, with one air-fluid level in the lower lobe. There was no history of foreign body aspiration, and the tuberculin test was negative at 1:1,000. She responded well to sulfadiazine and penicillin therapy. On March 28, 1947, the patient's right

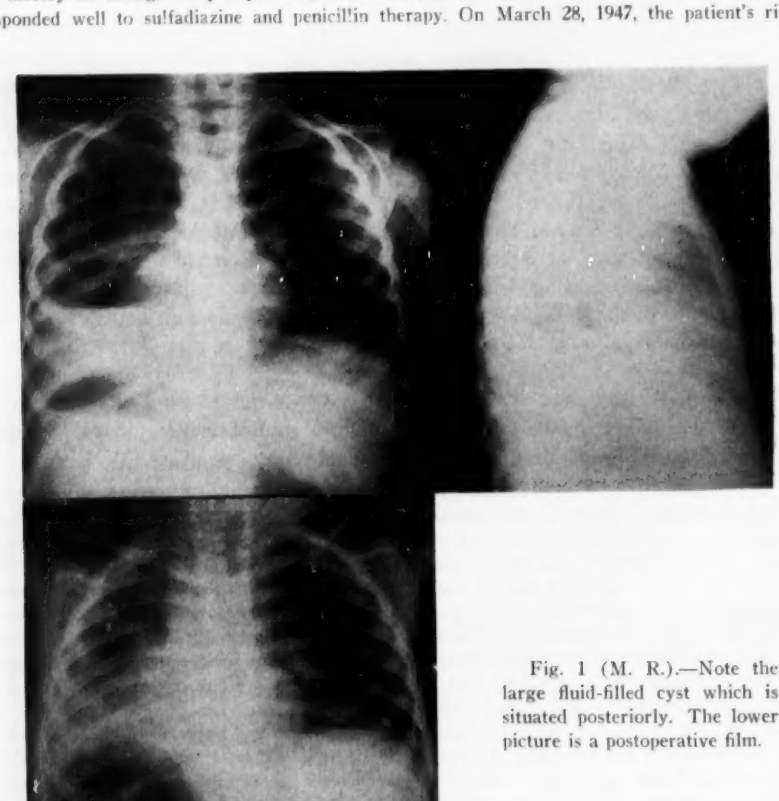

Fig. 1 (M. R.).—Note the large fluid-filled cyst which is situated posteriorly. The lower picture is a postoperative film.

chest was explored. The entire right lower lobe was nonaerated and infiltrated and contained at least one large cyst. In addition, a large artery entered the lower medial portion of the lobe. The artery came from the aorta in the region of the diaphragm. Grossly the lung was found to contain a large, multiloculated cyst about 5.5 by 7.5 by 2 cm. in size. In addition, there were several smaller cysts. There was no normal lung tissue present. Microscopically the cyst lining was composed of cuboidal or columnar epithelium. Only small areas were ciliated and pseudostratified.

Comment.—We consider this case a good example of intralobar pulmonary sequestration.

CASE 3.—B. H., a 14-year-old white boy, was referred to Bob Roberts Memorial Hospital with a four-and-a-half month history of chronic cough, productive of foul sputum. On admission he did not appear to be ill. Physical examination was essentially normal, as was the routine laboratory work. Tuberculin skin test was negative. X-ray of the chest revealed what appeared to be an area of pneumonitis in the right lower lobe. On bronchoscopy, pus was seen coming from the right lower lobe orifice. A bronchogram was done but was unsatisfactory. On Sept. 10, 1947, the patient underwent right exploratory thoracotomy. The right lower lobe was infiltrated and atelectatic. In addition, there was a large artery arising from the aorta in the region of the diaphragm, which entered the posterior medial portion of the lower lobe. The lower lobe was

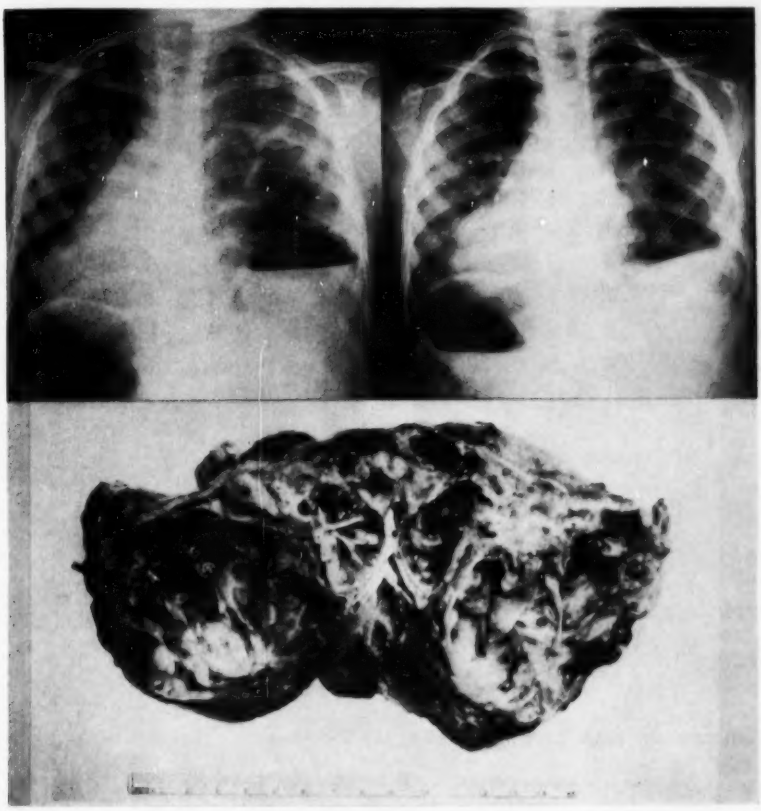

Fig. 2 (A. N.).—Note the large fluid-filled cyst, in addition to several air-filled cysts, in the right lower lung field in the preoperative (left) film. The other film was taken after the right lower lobectomy. The opened specimen shows the large cysts, in addition to several smaller ones.

firm and fibrotic with a thickened pleura. The cut surface showed many small cystic areas, some of which contained pus. No aerated lung could be seen. Microscopically the small cystic areas were lined by cuboidal epithelium. The remainder of the lobe showed severe chronic inflammation.

Comment.—This patient, too, demonstrates the disease, intralobar pulmonary sequestration, which was cured by surgical extirpation.

CASE 4.—P. J., a 22-month-old Negro girl, came to the University of Chicago Clinics with a history of several convulsive episodes, in which there was gagging, salivation, pallor, leg rigidity, and convulsive "beating" motions of both arms, lasting a few seconds and followed by a chill and

empty staring for one hour. These attacks were followed the next day by fever of 39.0 C. and coryza of several weeks' duration, with daily afternoon temperature elevations. At our institution neurological examination was negative. Studies for tuberculosis were also negative. The x-ray of her chest was reported as showing a "roentgenographically normal heart . . . a pulmonary infiltrate in the right lung field adjacent to the cardiac border, probably with an element of atelectasis, causing mediastinal shift to the right." Bronchoscopy was not helpful. Bronchography demonstrated upward and lateral displacement of the bronchi on the right, with missing right upper and middle lobe bronchi and probable atelectasis of a segment of the right lower lobe. A right exploratory thoracotomy was performed. The right pleural space was found to be entirely obliterated by pleural adhesions, with the pulmonary tissue appearing partially atelectatic. After the adhesions were freed, the lung expanded in the normal fashion. However, the lung was observed to consist of only a lower lobe with a pulmonary artery and one pulmonary vein. There were, in addition to the normal vessels, two large arteries, each 3 to 4 mm. in diameter, and

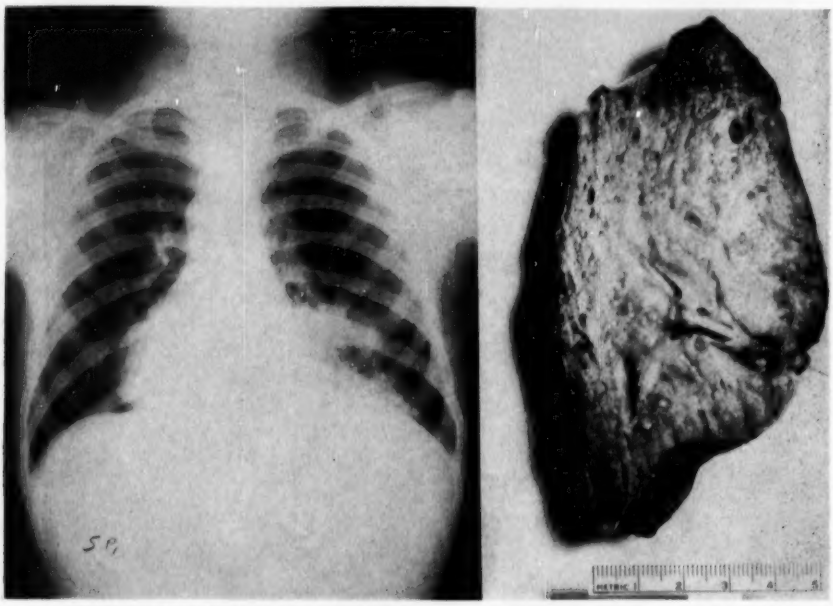

Fig. 3 (B. H.).—This film shows a nondiagnostic mass in the right lower lung field. The cut specimen demonstrates the large number of small cysts. The pointer is in the abnormal artery.

several smaller vessels running through the diaphragm to the inferior surface of this lobe. It was finally elected to do nothing with the anomaly. The recovery was uneventful. The chest was essentially unchanged in roentgenographic appearance postoperatively.

Comment.—This case will be discussed together with Case 5.

CASE 5.—S. P., a 4½-year-old Negro girl, was presented at Bob Roberts Memorial Hospital as having "asthma" of four years' duration. She had been well the first two months of her life, at which time she developed a febrile illness with respiratory distress which was diagnosed as pneumonia and treated at home with penicillin. The parents were informed at this time that her heart was shifted to the right, although no chest x-ray had been secured for confirmation. Dating from this illness and continuing until her admission here, four years later, she had intermittent attacks of wheezing, labored respirations, cough, and a temperature of 39.0 C. Between the attacks the child appeared perfectly well and active. An x-ray at 6 months of age, following a shoulder injury, revealed right mediastinal shift with presumed atelectasis. The routine laboratory

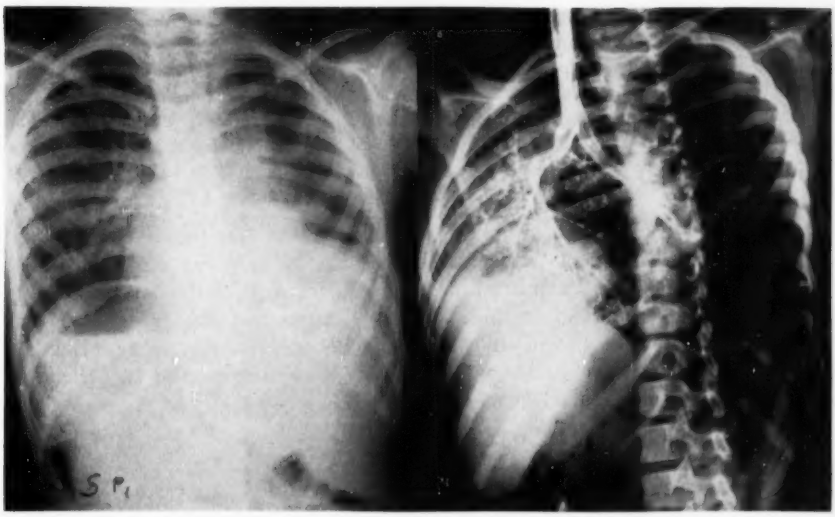

Fig. 4 (P. J.).—Note the right mediastinal shift. The oblique bronchogram demonstrates no evidence of normal upper or middle lobe orifices.

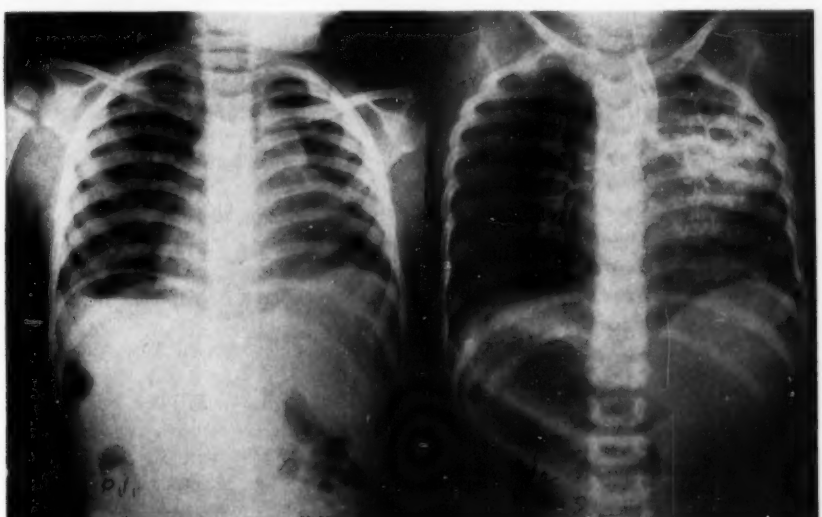

Fig. 5 (S. P.).—Note, again, the rather marked right mediastinal shift. The bronchogram shows upward displacement of the right main stem bronchus with no upper or middle lobe orifice.

work at our institution was within normal limits. The admission diagnosis was atelectasis of the right lower lobe due to underlying chronic pulmonary disease. Bronchoscopy and bronchography revealed a right lung anomaly consisting of agenesis of the right upper and middle lobes. At surgery this anomaly was confirmed. The lower lobe, which filled the hemithorax, was bound down with pleural adhesions to the diaphragm, which had two areas of eventration bulging into the chest. The liver underlay these eventrations, which were repaired. Several systemic vessels entered the inferior surface of the right lower lobe and appeared to arise from the aorta. As in the preceding case, nothing was done about the lung anomaly. The recovery was uneventful. On her last examination the patient was found to have a right hemithorax which was smaller than the left. There were no infiltrates in the lungs, and the child appeared perfectly well and was fully active. She had had no more of the respiratory infections.

Comment.—The last two cases are presented because, like the first three, they had vessels arising from the aorta. Unlike the first three, there was agenesis of the upper and middle lobes, instead of cystic malformation of the portion of lung where the anomalous vessel emptied. Morton, Klassen, and Baxter [19] report two cases with agenesis of the upper and middle lobes. However, they make no mention of an anomalous blood supply. Probably the systemic blood supply to the lung should have been ligated in these two cases.

SUMMARY

Three cases of intralobar pulmonary sequestration and two cases of agenesis of the right upper and middle lobes with anomalous systemic vessels are presented. Pulmonary sequestration is defined as the occurrence simultaneously of an area of congenital cystic lung with possible absence of communication with the normal bronchi and an aberrant artery running from the descending aorta to the lung parenchyma. The theories explaining its occurrence are discussed, along with its diagnosis and treatment.

Eleanor M. Humphreys, Professor of Pathology, offered many helpful suggestions.

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SUBTOTAL COLECTOMY WITH ILEOSIGMOIDOSTOMY AND FULGURATION OF POLYPS IN RETAINED COLON

Evaluation As Method of Treatment of Polyposis (Adenomatosis) of Colon

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POLYPOSIS (adenomatosis) of the colon requires surgical treatment because malignant degeneration will occur in at least a large percentage and possibly in all patients if the polyposis is not adequately treated. At present there are two principal alternative methods of treating this disease, namely, total colectomy with permanent ileostomy or subtotal colectomy with ileosigmoidostomy (or ileoproctostomy) and fulguration of polyps in the distal colon.

The procedure of total colectomy has the obvious advantage of removing all potentially malignant bowel tissue but has the equally obvious disadvantage of necessitating a permanent ileostomy. On the other hand, the procedure of subtotal colectomy with ileosigmoidostomy and fulguration of polyps in the distal remaining colon has the advantage of preserving a continent anal sphincter and the disadvantage of leaving in situ some potentially malignant colon tissue. If a portion of the colon is left, then the patient must be examined proctosigmoidoscopically at frequent intervals for the remainder of his life so that recurrent or new polyps may be removed in toto for biopsy or fulgurated.

Hoxworth and Slaughter,[1] in 1948, reviewed the American literature concerning this disease and listed the following factors which they considered favoring the use of one or the other of these two operations.

Factors favoring total colectomy:

1. Presence of carcinoma in rectum or rectosigmoid
2. Closely set polyps with marked hyperplasia and ulceration
3. Improbability of prolonged follow-up studies on the lower segment

Factors favoring sphincter preservation:

1. Absence of carcinoma in rectum or rectosigmoid
2. More sparse distribution of polyps in lower segment
3. Cooperative patient and facilities for prolonged follow-up

Hoxworth and Slaughter collected 17 cases from the American literature since 1930 in which the procedure of subtotal colectomy, ileosigmoidostomy, and fulguration of polyps in the remaining colon had been utilized in the treatment of polyposis of the colon. In their collected series, 4 of the 17 patients treated by this method died of cancer of the rectum from one to six years after fulguration was begun. These

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authors suggest that the lack of effectiveness of this method of treatment in these four cases may largely have been due to the relatively long interval between fulguration and subtotal colectomy (one to five years). They emphasize that once the rectum is clear of polyps and ileal anastomosis has been performed, repeated examination of the retained colon for biopsy and/or fulguration of recurrent polyps is necessary.

It is obvious, then, that retention of the distal large bowel entails a certain degree of risk with respect to the development of cancer of the colon. If that risk is slight, then the great majority of intelligent patients to whom the alternative procedures are honestly presented by the surgeon will probably choose the operation which permits preservation of the normal route of defecation. The desire of a patient to preserve the normal excretory function is easily understandable and should not be lightly dismissed by the surgeon as simply a sentimental attachment on the part of the patient. If, on the other hand, such a procedure is followed by the development of an appreciable incidence of carcinoma in the retained colon, then the surgeon must preferentially advocate and utilize the more radical procedure of total colectomy.

Twelve patients with polyposis of the colon treated by subtotal colectomy, ileosigmoidostomy, and fulguration of the distal colon have been studied at the University of Illinois Research and Educational Hospital and the Hines Veterans Administration Hospital since 1944.

REPORT OF CASES

CASE I.—C. S., a married white woman, 30 years of age, was first examined in the outpatient clinic of the University of Illinois Research and Educational Hospitals on March 29, 1943. She complained at that time of daily bloody stools for the last five years. Proctosigmoidoscopic and roentgenologic examination at that time showed evidence of polyposis of the colon with minimal involvement of the rectum, rectosigmoid, and right colon and maximal involvement of the transverse, descending, and sigmoid colon. Biopsies of numerous polyps were done and the lesions reported as benign.

On three occasions the patient was admitted to the hospital for proctoscopic fulgurations. She became pregnant, and no further treatment was given during pregnancy. In October, 1944, the patient gave birth to a normal male infant and after delivery noted increasingly frequent abdominal pain, which gradually progressed to bloody diarrhea. Upon admission to the hospital for definitive treatment of polyposis, the patient was pale, undernourished, and underweight. Laboratory studies revealed a severe secondary anemia, 2,500,000 RBC, with 8 gm. of hemoglobin per 100 cc. She was having 8 to 10 grossly bloody stools daily.

After preoperative preparation, on March 21, 1945, all polyps in the rectum and rectosigmoid for a distance of 24 cm. were destroyed by fulguration. On March 24, 1945, a subtotal colectomy was performed, with preservation of the cecum and the rectosigmoid 4 in. (10 cm.) above the peritoneal reflection. Postoperative course was uneventful. Pathological examination revealed no malignant lesion, and there were no polyps near the resected end of the colon.

The patient has been followed systematically at regular intervals and has regained normal weight and is living a normal life. The anastomosis, as well as a small portion of the cecum, can be visualized by the proctosigmoidoscope. Polyps have been seen on examinations on April 16, 1948, July 14, 1948, and April 6, 1949, and were destroyed by fulguration or removed *in toto* for biopsy. Air-contrast barium enemas have been performed periodically and reported as normal. On the last follow-up examination, on Jan. 21, 1954, no polyps were found.

Comment.—There is no familial history of polyposis of the colon. The cecum was preserved to maintain the dehydrating function, as the surgeon felt that an ileosigmoidostomy would produce diarrhea and possible persistence of the symptoms which made this patient so ill prior to surgery. As the cecum was retained, it is

necessary to use a 30-cm. proctosigmoidoscope, supplemented by periodic air-contrast barium enemas, to examine the colon for the presence of polyps. (This case has previously been reported by Hoxworth and Slaughter and is reported here for purposes of follow-up.)

CASE 2.—J. D., a 25-year-old white man, was admitted to Hines VA Hospital on July 18, 1946, with a history of rectal bleeding for one year and weakness and vague lower abdominal pain of about three months' duration. His family history revealed death of his grandfather and father of carcinoma of the bowel. One aunt was also known to have had diffuse polyposis of the colon. Diagnostic work-up, including proctosigmoidoscopy and air-contrast barium enema, confirmed the diagnosis of diffuse polyposis of the colon. Surgery was recommended but was deferred at the patient's request, and he was discharged on Aug. 30.

In July, 1947, he was admitted to the surgical service of the Kern General Hospital, and a subtotal colectomy and ileosigmoidostomy were performed by Dr. Earl J. Boehme.[2] Pathological examination of the resected segment was reported as showing no evidence of malignancy. The patient had postoperative fulguration of residual polyps until the rectum below the anastomosis was clear of polyps. On April 21, 1950, many (30) tiny polyps were fulgurated, again with complete removal of all polyps up to the ileum; examination on Aug. 8, 1951, revealed 7 or 8 tiny polyps in the region of the ileocolic anastomosis.* The patient was next seen at the VA Hospital in Dwight, Ill. on April 9, 1952, complaining of pain in the left thigh. Investigation revealed metastatic carcinoma to the femur and pelvis. The primary lesion was not located. On Aug. 19, 1952, he was transferred to Hines VA Hospital, where he received palliative deep x-ray therapy and further diagnostic study failed to reveal a primary lesion. On Sept. 29, 1952, he had an anterior lateral chordotomy for relief of intractable pain and was discharged on Sept. 13, 1952. He was readmitted on Jan. 20, 1953, with a pathological fracture of the right femur. He died of carcinomatosis on March 16, 1953. Permission for postmortem examination was refused.

Comment.—This case was previously reported by Dr. Earl J. Boehme and is presented here for follow-up purposes. While no primary lesion was discovered during the patient's hospitalization at the VA Hospitals at Dwight and Hines, in reviewing the records, it is noted that the lesion was an adenocarcinoma of the type derived from colonic mucosa. Proctosigmoidoscopic examination also revealed several large sessile polyps in the retained segment of rectosigmoid, and biopsy specimens were reported as not malignant. However, it is possible that in one of these sessile polyps, the biopsy tissue was not taken deep enough and that malignant degeneration had occurred in its base.

CASE 3.—J. L., a 31-year-old white man, was admitted to the Hines VA Hospital on Oct. 19, 1946, complaining of intermittent diarrhea and occasional cramp-like abdominal pain since 1942. Diagnostic studies, including proctosigmoidoscopic examination and air-contrast barium enema, revealed polyposis involving the entire colon. Fulguration of the rectal polyps was done in stages, and definitive surgery was deferred by the patient until Oct. 8, 1947, at which time a left hemicolectomy was performed. On Nov. 26, 1952, a right hemicolectomy and ileosigmoidostomy were performed. Pathologic examination of the resected colon revealed only polyposis.

The patient has continued faithfully to observe his follow-up periods. Periodic fulgurations have been necessary. His last admission was on Jan. 9, 1954. Several small polyps were seen on proctoscopy.

CASE 4.—P. C., a 33-year-old white man, was admitted to Hines VA Hospital on July 4, 1947, with a complaint of diarrhea and occasional rectal bleeding for a period of two and one-half years. Barium enema prior to his hospital admission had been reported as revealing a tumor of the descending colon. There had been no weight loss. The family history was negative for

* Boehme, E. J.: Personal communication to the authors, May 24, 1954. Reference 2.

polyposis. Diagnostic studies confirmed the presence of an obstructive lesion of the descending colon and revealed, in addition, diffuse polyposis. Proctosigmoidoscopic examination revealed only two sessile polyps within 25 cm. of the anal margin.

On July 28, 1949, a tumor of the sigmoid colon was resected. The pathological diagnosis was adenocarcinoma and multiple small polyps. On Nov. 10, 1949, a left hemicolectomy and ileosigmoidostomy were performed. On Feb. 9, 1950, a right hemicolectomy was performed. Pathological examination of the specimens revealed no additional malignant degeneration. Polyps were present in all sections of the colon. After fulguration of the rectal polyps, the patient was discharged on Feb. 20.

Since then the patient has been followed by his private physician and proctoscoped at three-month intervals. At our request, the patient was admitted to the VA Hospital at Jefferson Barracks, Mo., on Nov. 23, 1953, for follow-up examination, which revealed a sessile polyp at 10 cm. and several smaller polyps in the retained colon. The proximal portion of the colon could not be visualized with an ordinary proctoscope. Therefore, on Dec. 14, 1953, a revision of the ileosigmoidostomy was performed, with the anastomosis made at 9 in. (22 cm.) from the anus. The patient is now being followed at 3-month intervals at the VA Hospital at Jefferson Barracks, Mo.

Comment.—This patient illustrates an important point in surgical technique, namely, that the ileosigmoid anastomosis should be made at a level within reach of an ordinary proctosigmoidoscope (25 cm. from the anus). If the anastomosis is not so placed initially, further major surgery will be needed if the patient is to be adequately followed by periodic examinations of the remaining colon.

CASE 5.—A. R., a 27-year-old white man, was admitted to the Hines VA Hospital on Jan. 22, 1949, with complaints of diarrhea since April, 1948, and a 10 lb. (4.5 kg.) weight loss in the month immediately preceding admission. The family history was negative for polyposis. Work-up studies revealed diffuse polyposis of the entire colon and moderate secondary anemia. On March 15, 1949, right hemicolectomy and ileosigmoidostomy were performed, and on April 19, 1949, a left hemicolectomy was performed. The postoperative course after both surgical procedures was uncomplicated. No carcinoma was found in the resected colon.

Since surgery, the patient has had multiple-stage fulguration of polyps of the rectosigmoid. Although persistent efforts have been made to perform periodic examinations, the patient has cooperated only intermittently. He is last known to have been examined in June, 1952, in the VA Hospital at Fort Miley, San Francisco. He is now living in the Chicago area, but repeated attempts to have him report to the Hines VA Hospital for follow-up examination have been unsuccessful. It has been established that the patient was alive as of October, 1953.

CASE 6.—E. C., a 31-year-old white man, was admitted to the Hines VA Hospital on July 17, 1950, complaining of recurrent bouts of rectal bleeding, abdominal pain, and distention since 1943. He stated that in 1944 rectal polyps were removed through a proctoscope and that since that time he had continued to have abdominal cramps and diarrhea. Proctosigmoidoscopic examination and air-contrast barium enema revealed polyposis involving the entire colon. On Aug. 16, 1950, and Aug. 31, 1950, fulguration of the polyps in the rectum was done. On Nov. 1, 1950, resection of the terminal portion of the ileum and colon down to the lower rectosigmoid was performed and continuity was reestablished by means of ileosigmoidostomy. The postoperative course was uneventful.

He has been followed at regular intervals by this and other Veterans Administration Hospitals. The last follow-up examination (Sept. 8, 1953), at the Veterans Administration Hospital, Iowa City, revealed polyps in the rectosigmoid, which showed active growth on microscopic examination. Fulgurations were performed.

CASE 7.—R. L., a 32-year-old white man, was admitted to Hines VA Hospital on March 15, 1944. He had had an ileostomy performed on March 19, 1943, while in service for "ulcerative colitis." He was transferred to the VA Hospital at Hines with a diagnosis of ulcerative colitis and psychosis with mental deficiency. As this patient was a foster child, no family history was obtainable.

Diagnostic studies revealed diffuse polyposis of the colon. Ileosigmoidostomy was performed on May 26, 1944, followed by a subtotal colectomy on July 8, 1944. On Oct. 12, 1944, he was transferred to the VA Hospital in Knoxville, Iowa, for custodial care.

The patient apparently did well until December, 1946, when a bowel obstruction developed, and he died on Jan. 5, 1947. Postmortem examination was not performed. Clinically, however, the patient was thought to have developed bowel obstruction secondary to adhesions, and not due to carcinoma. There is no record of fulguration of any polyps after his transfer to Knoxville.

CASE 8.—W. B., a 23-year-old white man, was transferred to Hines VA Hospital from the VA Hospital in Wadsworth, Kan., on Oct. 31, 1945, with the diagnosis of benign polyps of the rectum. He gave a history of frequent bowel movements of soft consistency, numbering six to eight a day the preceding summer. He had also noted cramping lower abdominal pain, intermittent rectal bleeding, and a 40 lb. (18 kg.) weight loss in the preceding 18 months. He was chronically ill and undernourished, without specific physical findings. The family history was negative for polyposis. Proctosigmoidoscopy and air-contrast barium enema revealed diffuse polyposis of the colon.

On Jan. 25, 1946, ileostomy and right hemicolectomy were performed. Pathological examination of the resected specimen revealed malignant degeneration of the polyps of the transverse colon with extension into the mesentery.

Patient was readmitted on May 25, 1946. After fulguration of rectal polyps, subtotal colectomy was completed, with anastomosis of the ileum to the sigmoid. At surgery, no further evidence of malignancy was found.

Since discharge from the VA Hospital at Hines he has been followed fairly regularly at various VA facilities in the region of his home and by letter from this hospital. He is able to work; he complains of some cramping abdominal pain and occasional rectal bleeding. The last follow-up examination, at the VA Hospital in Wadsworth, Kan., on June 3, 1953, revealed no polyps.

CASE 9.—W. C., a 26-year-old white man, was admitted to Hines VA Hospital on April 30, 1951, with complaints of intermittent rectal bleeding and diarrhea since 1944. Diagnosis of polyposis of the colon had been established prior to admission and was confirmed here by proctosigmoidoscopy and air-contrast barium enema. The family history revealed that his father had died at the age of 41 of carcinoma of the rectum.

On May 10, 1951, a subtotal colectomy with ileosigmoidostomy was performed. Pathological examination of the specimen revealed no malignant degeneration.

Follow-up study at the VA Hospital in Indianapolis, Nov. 13, 1951, revealed numerous small polyps in the remaining rectosigmoid colon. Since this follow-up, attempts to have the patient report to VA installations for examinations have failed. However, letter follow-up has been maintained, and the patient is reported to have gained 30 lb. (13.6 kg.) in weight, to be working regularly, and to be asymptomatic except for occasional episodes of diarrhea following dietary indiscretion.

CASE 10.—J. M., a 58-year-old white man, was admitted to the University of Illinois Research and Educational Hospitals on Aug. 29, 1951, with the history of having had a rectal polyp fulgurated in 1948. In 1950 a polyp was removed from the sigmoid and reported as "potentially malignant." Proctosigmoidoscopy on July 18, 1951, revealed no polyps. X-rays confirmed that the patient had polyposis of the colon.

On Sept. 14, 1951, the patient underwent a subtotal colectomy with resection of the hepatic flexure, transverse colon, and descending colon, and anastomosis of the ascending colon to the rectosigmoid. X-rays on July 9, 1952, revealed multiple polyps within the residual colon. However, proctoscopic examination was negative. The patient was readmitted to the hospital, and a resection of the ascending colon and sigmoid colon with an ileosigmoidostomy was performed on Aug. 11, 1952. The patient has been followed regularly since surgery, and at no time, through Feb. 17, 1954, have polyps been demonstrated in the retained segment of rectosigmoid.

Comment.—It is interesting to note that this man, whose family history was negative, is one of the oldest patients with diffuse polyposis reported in the literature

in whom a frank malignant condition was not found. This case again illustrates the advisability of initially removing all of the colon except that which can be examined with a standard 25-cm. proctosigmoidoscope.

CASE 11.—G. D., a 38-year-old white man, was admitted to Hines VA Hospital on the advice of his private physician, who had discovered a carcinoma of the colon secondary to polyposis in an older brother. A younger brother and a sister also had polyposis. The patient's mother had died of carcinoma of the colon. Physical examination and work-up confirmed the diagnosis of polyposis of the colon.

On Sept. 10, 1953, subtotal colectomy with ileosigmoidostomy was performed. The postoperative course was uneventful, and the patient was discharged on Sept. 22, 1953. On Nov. 11, 1953, fulguration of residual polyps was commenced. Additional polyps were fulgurated on Dec. 9, 1953, and in March, 1954. At the last examination, in March, only a few polyps were found and fulgurated.

CASE 12.—J. D., a 33-year-old white man, a brother of the patient in Case 11, was admitted to Hines VA Hospital on Aug. 26, 1953. At the time of admission, he was asymptomatic. Physical examination and diagnostic studies revealed polyposis without evidence of malignant degeneration.

On Sept. 19, 1953, subtotal colectomy with ileosigmoidostomy was performed. Postoperative course was uneventful. Fulguration of the very extensive polyposis of the retained segment was begun on Nov. 12, 1953. Three additional fulgurations were performed on Dec. 10, 1953, Jan. 7, 1954, and in March, 1954. At the last examination, in March, 1954, only a few small polyps were found.

COMMENT

Two of the 12 patients of this series have died since operation. One patient died of bowel obstruction clinically thought to be secondary to adhesions, and not to carcinoma, although postmortem examination was not performed. One patient (Case 2) died of carcinomatosis. Although no primary lesion was discovered, the metastatic carcinoma was an adenocarcinoma of the type derived from colonic mucosa. It is to be noted that 2 of the 10 living patients in this series have failed to report for periodic examinations, despite the fact that persistent efforts have been made to have them do so. This must be recognized as a danger inherent in this method. Eight of the 10 living patients of our series have regularly reported for their periodic follow-up examinations. Two of these patients have just recently finished the initial series of fulgurations of the retained colon. The remaining six patients have been followed for 106, 84, 35, 23, 19, and 13 months, respectively, without the development of carcinoma of the colon being noted.

COLLECTED CASES

We have been able to collect 122 cases from the American surgical literature (including the present series) in which the use of subtotal colectomy, ileosigmoidostomy, and fulguration of the lower colon in the treatment of polyposis of the large bowel has been reported. These collected cases are listed in Table 1. In 12 patients of this collected series, carcinoma of the colon developed after surgical treatment of polyposis of the colon by subtotal colectomy, ileosigmoidostomy, and fulguration. Analysis of the case reports of these 12 patients indicates that in 1 patient carcinoma was already present at the time of the initial fulguration, and in 5 patients the case reports actually state or suggest (by lack of mention) that the patients had not had periodic examination of the retained colon after performance of the initial operation. In four of these five patients carcinoma of the colon was found 8, 6, 17, and 8 years, respectively, after the operative procedure. (In one of the patients the time interval between surgery and the appearance of carcinoma of the colon was not given.) In

six patients the case reports stated that the patients had had periodic examination of the retained colon. In four of these patients carcinoma of the colon was noted four, three, one, and two years, respectively, after operation. (In two patients the interval between surgery and the appearance of carcinoma of the colon was not stated.) In one of these six patients (collected Case 17), evidence of metastatic carcinoma developed three years after surgery, the author attributing this to a small carcinoma which had probably been overlooked in the resected colon. However, this patient had several sessile polyps fulgurated one year after the original surgery, and it is possible that the carcinoma may have been present in one of these polyps.

Thus, 12 patients of the collected series developed carcinoma of the colon after the procedure of subtotal colectomy, ileosigmoidostomy, and fulguration of the remaining colon. However, in only six of these patients did carcinoma develop while the patient was stated to be under periodic follow-up care. Although failure of the patient to report regularly for follow-up examination must be regarded as a hazard of the method of treatment, the development of carcinoma in such a patient should not necessarily be regarded as evidence of failure of the method of treatment. Just as the medical patient who fails to take the medication prescribed by his physician cannot properly be considered to represent a failure of that type of medical treatment, so a patient with polyposis of the colon who does not follow the surgeon's instructions to report for periodic follow-up examinations and who develops carcinoma of the retained colon should not be considered a failure of this type of surgical treatment, since regular examination and fulguration of the distal colon after the primary operation are integral parts of the method of treatment. The finding of a carcinoma of the colon years after the initial surgery in a patient who failed to report for regular examination and treatment of the distal colon may properly be considered an instance of failure of patient cooperation rather than failure of the method of treatment.

When the one patient in whom carcinoma of the colon was present initially and the five patients who apparently did not follow the outlined method of treatment are omitted from the evaluation of the method of treatment, it is noted that carcinoma of the colon developed in 6 of 115 collected cases, an incidence of 5.2%. It is to be noted that, unfortunately, four of the six patients who developed carcinoma of the colon while under periodic follow-up care had metastases present at the time the diagnosis of carcinoma was made.

The duration of follow-up examination in these 115 collected cases is summarized in Table 2. Although only 3 of these patients had been followed for 15 years or more at the time of the original reports, 32 patients had been followed for five years or more. Forty-one patients had been followed for three years or more, and 58 patients were reported to have been followed less than five years. The length of follow-up was not stated for 25 patients. Although the length of follow-up care is short, in many instances it is to be noted that the development of carcinoma of the colon was not reported in any patient regularly followed more than four and a half years by periodic examination of the lower colon and fulguration of new or recurrent polyps. This finding is not, however, to be construed to mean that periodic examination of the lower segment of the colon may be discontinued after this period of time, for carcinoma of the colon did occur from 6 to 17 years after surgery in patients who apparently did not report for periodic inspection and fulguration of the lower colon.

TABLE 1.—*Collected Cases of Polyposis of Colon Treated by Subtotal Colectomy, Ileosigmoidostomy, and Fulguration of the Retained Colon**

Case No.	Author	Location of Carcinoma	Result	Length of Follow-Up	Comment
1	Lilienthal [3]	None	Good	19 yr.	.....
2	Rankin [4]	None	Good	2 yr.	.....
3	Hickman [5]	None	Good	2 yr.	.....
4	Pfeiffer and Patterson [6]	None	Good	1 yr.	.....
5	(Same)	None	Good	1 yr.	.....
6	Pugh and Nesselrod [7]	None	Good	Not given	.....
7	Guptill [8] Case 3	None	Died of carcinoma	4½ yr.	Carcinoma found 4½ yr. postoperatively; abdominal-perineal resection performed; died 5½ yr. after original surgery of carcinoma
8	Case 4	None	Good	7 yr.	.....
9	Johnson [9]	None	Good	3½ yr.	.....
10	Ravitch and Sabiston [10]	None	Died of carcinoma after abdomino-perineal resection	8 yr.	Fulguration, 1937; ileosigmoidostomy, 1937; returned Feb., 1945, with carcinoma of rectum and abdominal-perineal resection performed; died 8 mo. later
11	Best [11] Case 4	Rectum	Good	2 yr.	Case included despite presence of carcinoma at time of surgery because of 2-yr. follow-up
12	Estes [12]	None	Good	3 yr.	.....
13	Gardner [13]	None	Good	1 yr.	.....
14	Gardner	None	Good	Not given	.....
15	Gardner	None	Good	Not given	.....
16	Jones and Turnbull [14]	None	Good	2 yr.	.....
17	Jones and Turnbull [14]	None	Carcinomatosis-developed 3 yr. postop.	3 yr.	Surgical specimen reported as negative for cancer; sessile polyps were fulgurated 1 yr. later; developed evidence of metastatic carcinoma 3 yr. after surgery; author attributes metastasis to small carcinoma overlooked in resected colon; however, carcinoma may well have been in sessile polyps fulgurated 1 yr. after original surgery
18	Rankin and Webb [15] Case 3	None	Good	5½ yr.	.....
19	Case 4	None	Good	5½ yr.	.....
20	Case 5	None	Good	10 yr.	.....
21	Case 8	None	Good	7 yr.	.....
22	Case 9	Hepatic flexure	Good	6 mo.	.....
23	Case 10	Right colon	Good	6 mo.	.....
24	Scarborough and Klein [16]	None	Good	10 yr.	.....
25-27	Scarborough and Klein [16]	None	Good	Not given	.....
28	Schutte †	None	Carcinoma developed in retained colon	8 yr.	Carcinoma of sigmoid 8 yr. after operation; had not been examined for 2 yr.
29	Schutte	None	Carcinoma developed in retained colon	Not given	Had not reported for periodic examination; inoperable carcinoma of sigmoid with metastases
31	Boehme [2] Case 2	None	Good	Not given	.....
32	Case 4	None	Good	Not given	.....
33	Case 5	2 malignant polyps	Good	Not given	.....
34	Case 6	3 polyps—carcinoma in situ	Good	Not given	.....
35	Case 7	Transverse colon	Good	4 mo.	.....
36	Clark and Parker [17]	None	Good	1 yr.	.....
37	Howard and Trent [18]	None	Good	Not given	.....
38	Reichman [19]	None	Good	Under 9 mo.	.....
39	Anschuetz [20] Case 1	Two in colon 1937 and 1947	Good	18 mo.	.....
40	Case 2	None	Good	2 yr.	.....
41	Case 3	None	Good	3 mo.	.....
42	Mayo, DeWeerd, and Jackman [21]	None	Required abdominal-perineal resection	6 yr.	Carcinoma of rectum found 6 yr. after surgery; patient well 4 yr. after abdominal-perineal resection
43	Mayo, DeWeerd, and Jackman [21]	None	Required abdominal-perineal resection	1 yr.	Carcinoma of rectum found 1 yr. after surgery and an abdominal-perineal resection was performed

Case No.	Author	Location of Carcinoma	Result	Length of Follow-Up	Comment
44	Mayo, DeWeerd, and Jackman [21]	None	Required abdominal-perineal resection	17 yr.	Carcinoma of the rectum found 17 yr. after surgery and an abdominal-perineal resection was done; well 1 yr. after this surgery
45	Mayo, DeWeerd, and Jackman [21]	None	Died of carcinoma	2 yr.	Carcinoma found near anastomosis 2 yr. postop.; metastases also present at that time
46-80	Mayo, DeWeerd, and Jackman [21]	Cases not reported individually	Good in 35 cases	1 case, 18 yr. 4 cases, 10 yr. or more 11 cases, 5 yr. or more 10 cases, under 5 yr.	.....
81	Walton [22]	None	Good	Not given	.....
82	Walton [22]	None	Good	Under 2½ yr.	.....
83	Walton [22]	None	Good	Under 1½ yr.	.....
84	Harris and Hay [23]	None	Good	2 yr.	.....
85	Harris and Hay [23]	None	Good	3 yr.	.....
86	McRae [24] Case 6	Malignant polyp without invasion in specimen	Good	Under 2 yr.	.....
87	Case 10	None	Good	Under 18 mo.	.....
88	Case 11	None	Good	Under 18 mo.	.....
89	Case 12	None	Good	Under 18 mo.	.....
90	Schaeffer [25] Case 3	None	Good	2½ yr.	.....
91	Case 4	None	Good	Not given	.....
92	Gross [26]	None	Good	11 yr.	.....
93	Gross [26]	None	Good	12 yr.	.....
94	Gross [26]	None	Good	5 yr.	.....
95	Gross [26]	None	Good	3 yr.	.....
96	Gross [26]	None	Good	3 yr.	.....
97-108	Cattell [27]; Swinton and Doane [28]	None	Died of carcinoma	Not given	Despite careful follow-up, patient developed carcinoma, with metastases present at time of discovery of carcinoma
			Developed carcinoma in retained colon	Not given	Swinton and Doane [28] give these data in general discussion of polyps and state 2 patients of their series have developed carcinoma in the stump; presumably this is a later follow-up on one of the cases tabulated by Cattell [27]
109	Tumulo [29]	None	Good	1 yr.	.....
110	Hoxworth and Slaughter [1] Case 6 (Case 1, this report)	None	Good	9 yr.	.....
111	Boehme [2] Case 3 (Case 2, this report)	None	Died of carcinoma	4½ yr.	Found to have metastatic carcinoma 4½ yr. after surgery and died 1 yr. later; postmortem refused; clinical evidence that primary was in rectum
112	Dye and others [30] Case 3 (Case 3, this report)	Good	Good	7½ yr.	.....
113	Case 5 (Case 4, this report)	Sigmoid	Good	6 yr.	.....
114	Case 8 (Case 5, this report)	Sigmoid	Good	5 yr.	.....
115	Case 11 (Case 6, this report)	None	Good	3 yr.	.....
116	This report, Case 7	None	Died	3½ yr.	Patient died of bowel obstruction not clinically due to carcinoma
117	This report, Case 8	Malignant degeneration of polyps in transverse colon	Good	6 yr.	.....
118	This report, Case 9	None	Good	2½ yr.	.....
119	This report, Case 10	None	Good	2½ yr.	.....
120	This report, Case 11	None	Good	6 mo.	.....
121	This report, Case 12	None	Good	6 mo.	.....

* In 12 cases carcinoma apparently developed after completion of colectomy and iliosigmoidostomy (Cases 7, 10, 17, 28, 29, 42, 43, 44, 45, 97, 98, and 111).

† Schutte, A. G., cited in discussion of paper by Scarborough & Klein.[16]

A risk of approximately 5% that carcinoma of the colon will develop with this method of treatment does not seem to us to be incompatible with the advantage of preserving a continent anal sphincter. Moreover, the fact that metastases were already present when the diagnosis of carcinoma of the colon was ultimately made in four of six patients one to four and one-half years after subtotal colectomy, ileosigmoidostomy, and fulguration suggests that a small primary carcinoma with early metastases might possibly have been present at the time of the initial operation. If so, total colectomy might have been no more effective in controlling the metastatic lesions. This is, of course, an unprovable thesis, but it must be remembered that even in the absence of a known carcinoma of the colon, surgical treatment of polyposis of the colon by total colectomy may be followed in the early postoperative years by metastatic carcinoma secondary to unsuspected malignant degeneration in one of the hundreds of grossly normal polyps of the resected colon.

With this method of treatment, there is the added hazard that an occasional asymptomatic patient, despite the careful explanations and persistent efforts of the surgeon, will fail to report regularly for examination of the retained colon and for biopsy in toto or fulguration of new or recurrent polyps. That this is a real drawback to the effective utilization of the method of treatment cannot be denied. That the incidence of development of carcinoma of the colon in such patients who do not faithfully follow the treatment regimen will be appreciably higher is readily acknowledged. Yet it does not seem rational to subject all patients with this disease to the more radical procedure of total colectomy simply because a few recalcitrant patients may be expected to ignore their follow-up appointments.

TABLE 2.—*Length of Follow-Up of 115 Collected Cases**

Years	1 or Less	1-2	2-3	3-4	4-5	5-10	10-15	15 or More	Not Given
No. of cases	13	6	11	8	1	21	8	3	25

* Nineteen (19) cases reported as under 5 years

We are in agreement with the criteria of Hoxworth and Slaughter in making the decision as to which of the two principal alternative procedures should be utilized in the treatment of individual cases of polyposis of the colon. We feel, in addition, that those patients who meet the criteria for utilization of the procedure of subtotal colectomy, ileosigmoidostomy, and fulguration should be told of the approximate risk of developing cancer of the retained colon and of the need for periodic examination and treatment of the retained colon at three- to six-month intervals for the rest of their lives. Some of these patients may possibly elect to have total colectomy with permanent ileostomy performed because of the smaller risk of development of cancer and the absence of the need for continued treatment. Those patients who elect the sphincter-preserving operation should be made fully aware of the reason for regular follow-up examinations. If the patient does not meet the criteria for application of the less radical procedure, there is obviously no need for discussion of the two alternative procedures with him.

The necessity for periodic examination and treatment of the retained colon at three- to six-month intervals for the duration of the patient's life places a real responsibility on both the patient and the surgeon. Boehme [2] has suggested that the anastomosis of the ileum and colon be placed at a lower level than has formerly been the

common practice. With this concept we are in full agreement, and we believe that it is better to anastomose the ileum to the rectosigmoid at or just above the peritoneal reflection (approximately 15 cm. from the anus) rather than at a higher level, which requires the full length of the standard proctosigmoidoscope (25 cm.) for examination. An anastomosis of the ileum and colon at the level of the peritoneal reflection still permits utilization of the greater safety of the anterior serosal covering of the rectosigmoid in the performance of the anastomosis and yet leaves in situ a shorter length of potentially malignant colon, which can be more easily visualized and treated periodically than can a longer segment. In our experience, this shorter length of retained colon does not impair the continence of the anal sphincter or appreciably affect the character of the fecal discharge. Possibly, with the utilization of this principle, the incidence of development of carcinoma in the retained colon following treatment of polyposis of the colon by subtotal colectomy, ileosigmoidostomy, and fulguration of the lower segment will be further reduced.

SUMMARY AND CONCLUSIONS

Review of the cases of polyposis (adenomatosis) of the colon in this report and of those collected from the American literature which have been treated by the method of subtotal colectomy, ileosigmoidostomy, and fulguration of the retained colon indicates that there is to date a reported incidence of carcinoma of the colon developing after this method of treatment of 5.2% in 115 collected cases.

The requirement of periodic examination of the retained colon and biopsy or fulguration of new or recurrent polyps is an integral part of the method of treatment. The failure of an occasional asymptomatic patient to report regularly for examination and treatment of the distal colon is a hazard of the method of treatment and is associated with the development of a higher incidence of carcinoma of the colon.

We do not feel that the percentage risk of developing carcinoma of the colon after this method of treatment is incompatible with the advantage of preserving a continent anal sphincter, provided that the individual patient, first, meets the criteria of Hoxworth and Slaughter for utilization of this method of treatment and, second, faithfully reports for periodic examination and treatment of the retained colon for the duration of the patient's life.

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SURGICAL MANAGEMENT OF URINARY TRACT CALCULI

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HISTORY

IN THE ancient days, Egyptians and Hindus described urinary calculi and various types of lithotomy.[1] From the writings of Hippocrates, the operation was evidently performed in many instances by itinerant and unscrupulous practitioners. Hippocrates in his oath, about 400 B. C., stated, "I shall not cut for stones." It is, of course, not clear whether it was because the operation was followed so frequently by disastrous results or death, or whether it was that the Father of medicine did not wish to be classified with the type of practitioner who usually did lithotomy.

Through the centuries, much was written about urinary calculi, but little advance was made, either in the diagnosis or treatment, until Roentgen, in 1895, discovered the rays that bear his name. In 1896 McIntire described the diagnosis of urinary calculi by roentgenography, and Schmidt, in Chicago, was the first to employ a metallic wire inside the ureteral catheter to give an outline of the ureter. Woelker and von Lichtenberg used Collargal (colloidal silver) in 1906 to outline the kidney pelvis and ureter. In 1918 Cameron [2] advised the use of iodide solution as a contrast medium to delineate the urinary tract. Prior to that time, Collargal and thorium were used. Both these substances frequently caused untoward reactions when used for pyelography. A significant advance was made when Benz, in 1930, devised Iopax (Uroselectan) for intravenous pyelography.

During the last 20 years, both roentgenographic equipment and the opaque media have enormously improved. Although many problems remain to be solved, particularly the cause and prevention of urinary calculi, tremendous advances have been made in recent years by clinicians and research workers.

An outstanding and informative communication is a panel discussion on urolithiasis [3] at the 1953 Annual Meeting of the American Urological Association. Anyone interested in calculous disease should peruse this and other recent literature on the subject.

EXAMINATION AND DIAGNOSIS

An obstructing stone almost always causes severe renal colic. A nonobstructing stone may cause pain by irritation to the kidney or by infection. Differential diagnosis must be made of symptoms and pain caused by calculi and those caused by orthopedic, intestinal, neurologic, or pelvic conditions.

In examining for painful and tender areas, the examiner should pass his finger along the undersurface of the ribs on the painful side. By so doing, he will occa-

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sionally find that the patient's complaint is from an intercostal neuralgia. However, if the history and physical examination or urinalysis are suggestive of urinary tract disease, further study, such as excretory pyelography, is indicated. At the termination of this examination, one film should be exposed while the patient is in the upright position. Such a film will demonstrate whether the kidneys are draining. Likewise, if a nonopaque stone is present in the ureter, it can usually be visualized with certainty.

If an open operation is contemplated for the removal of calculi, faulty drainage other than that caused by the stone should be looked for. If such a mechanical stasis is present, it should, if possible, be corrected when the stone is removed. If there is faulty drainage of the renal pelvis, a suitable pyeloplasty or ureteroplasty should be performed. Likewise, if a calyx fails to drain well or its mucosa is indurated from the stone or infection, calycectomy or partial nephrectomy should be carried out when indicated. At times malposition of the kidney, such as ptosis, rotation, or torsion, is a causative factor in the formation of calculi. Therefore, when such a condition is present, nephropexy is indicated.

If infection is present, the identity of the pathogens should also be determined so that appropriate antibiotics can be used. Multiple stones or one that extends into two or more of the calyces should be removed only when roentgenographic equipment is available, so that films can be exposed at the operating table to determine the location and insure that all of the calculi have been removed.

INDICATIONS FOR INTERVENTION

A stone that is fast in the calyx or in the parenchyma of the kidney need not be removed, provided it produces no renal damage or foci of infection. A coral stone which fills the renal pelvis, with dendrites into the calyces, presents at times a difficult problem. The question arises, "Should we do nephrolithotomy, nephrectomy, or no operation at all?" The functional capacity of the involved kidney, the condition of the contralateral kidney, the symptomatology, and the presence or absence of infection, all must be considered. At times the excretory function of the kidney containing the coral stone is difficult to determine. However, there is a relation between the blood supply of a kidney and its function; therefore, arteriography (Fig. 1) is helpful in deciding whether the kidney should be saved or sacrificed. An arteriogram [4] also provides valuable information regarding the blood supply of the contralateral kidney. A stone that is free in the kidney pelvis, if it is too large to pass down the ureter, should be removed as soon as it is convenient to do so.

Many stones which enter the ureter pass into the bladder and are eliminated with the urine, provided the patient can tolerate the pain. Other stones pass into the lower ureter, from which they can be removed by cystoscopic manipulation. If a stone remains in the upper ureter and it is associated with several days of pain, the caliber of the ureter in relation to the size of the stone must be carefully considered before attempting manipulation.[3] Regardless of the location of the calculus, cystoscopic manipulation should be undertaken only when a roentgenogram and/or incision for drainage can be made if either or both procedures become indicated.

However, a calculus should not be left in the ureter indefinitely, for one of two complications may occur. After the ureter has been completely obstructed for several hours, the pain, and even the tenderness, ceases unless there is some release

of the obstruction. If complete obstruction is allowed to remain, the kidney becomes functionless permanently. The second complication is plastic infiltration and fibrosis of the ureteral wall. To gross appearance and to palpation, this type of fibrosis is suggestive of neoplasm except that the induration is smooth and extends several centimeters distally from the location of the stone. It has been my experience that if this process is at all extensive, the ureter remains malfunctioning after the stone has been removed, with resultant hydronephrosis and damage to the kidney, so that pyelostomy or nephrectomy becomes necessary. Only during the last few years have I encountered this type of inflammatory fibrosis of the ureter. I believe that before the days of effective antibiotics and urinary antiseptics the infection

Figure 1

became so overwhelming that the kidney was removed on the diagnosis of infected hydronephrosis or renal suppuration.

PROCEDURES

For the removal of stones from any portion of the kidney or upper ureter, an incision parallel to the 12th rib [6] extending from the border of the erector spinae muscle to the midclavicular line anteriorly usually suffices. If the patient is corpulent, a partial resection of the 12th rib facilitates exposure. Of course, the removal of stones from an extrarenal pelvis should be through a posterior pyelostomy. A coral stone with two or more dendrites into the calyces should be removed through an incision of the parenchyma at Brödel's * line. Before making an extensive incision into the renal parenchyma, a rubber-covered clamp, such as is used for

* References 3 and 5.

intestinal anastomosis, should be placed on the pedicle just taut enough to control the bleeding. Such a clamp can be left in place for at least one hour without danger of permanent damage to the kidney. In dealing with large stones in an intrarenal pelvis, the surgeon must carefully consider whether pelviolithotomy or nephrolithotomy will cause the less severe degree of trauma to the pelvic mucosa and parenchyma. An isolated stone in a calyx can usually be shoved into the pelvis by the blunt end of a straight needle or removed through the renal parenchyma with a small forceps.

After removal of all stones, verified by a roentgenogram, the bleeders on the cut surface of the kidney should be ligated by transfix 0000 plain absorbable surgical (gut) sutures and an Atraumatic needle. The clamp should not be released until all visible bleeders have been ligated,[5] the renal capsule sutured, and the mattress sutures completed. Not only the hemostasis but also the accurate reapproximation of the two halves of the kidney is important. A chromic 000 absorbable surgical (gut) suture should be used on an Atraumatic needle to close the capsule with a running lock stitch. After complete closure of the capsule, mattress chromic 00 or 000 absorbable surgical (gut) sutures on a straight needle should be used in figure-of-eight sutures about 1.5 cm. from the edge of the incision and about 1.5 cm. apart. If satisfactory tabs of fat are available, they can be used. Otherwise, ribbon catgut serves well when placed under the sutures to keep them from tearing the renal capsule. After an incision in the renal parenchyma of any extent, a nephrostomy drain should be used. A No. 24 F., 5-cc. bag catheter is satisfactory. If there has been a plastic operation on the renal pelvis or the upper ureter, it is advisable, in most instances, to use a splinting tube to fit the size of the ureter. If the pyeloplasty or ureteroplasty has been at all extensive, such a splinting tube should remain in place between five and six weeks.

As an additional safety factor against obstruction by clots, a posterior pyelostomy should be performed. Such an incision in the pelvis need not be sutured. It has been my practice not to suture an incision in the kidney pelvis or ureter unless it is for the purpose of holding edges in apposition or to prevent fat or other tissues from falling between the edges. If sutures are made to close an incision in the kidney pelvis or ureter, they should be placed in the adventitia only, never in the mucosa. Sutures placed in the mucosa are at times followed by urinary fistula, which persists until the sutures have been absorbed. The idea of not suturing such an incision I learned from Charles Mayo Sr. An incision in the renal pelvis or ureter should be carefully covered by fat. If at all possible, it should be a pedicle of fat.

After any open operation on the kidney or ureter, a tissue drain, either in the incision or in a stab wound, should be left in place at least six days. A practically nonobstructable drain, and one that is tolerated well by the tissues, can be made by splitting a small rubber tube and placing it inside a fenestrated Penrose drain. The loin incision should be closed by approximating the corresponding layers of muscle and fascia. Chromic absorbable surgical (gut) suture is usually satisfactory for the muscle and fascia, and nonabsorbable surgical (silk) suture for the skin.

Adequate extraperitoneal exposure of the lower ureter can be obtained by a transverse incision in the lower abdomen, through the skin, fat, and fascia. The rectus muscle can then be retracted and the peritoneum reflected off the pelvic wall.

After removal of the calculus, the incision in the ureter need not be closed. It should be covered by fat. Tissue drains should be used and the abdominal wall carefully closed.

Of the various types of equipment for cystoscopic manipulation of stones from the lower ureter, the Johnson stone extractor [7] is the most satisfactory. However, for this type of an extractor to be efficient, it should have a leader shaped the same as the point of a Wishard catheter. It is also extremely important that the basket be properly shaped before it is passed. It should be pear-shaped, with the base attached to the staff and the apex to the leader. The wires in the wide portion of the basket will then straddle the stone, which becomes encaged. The convergence

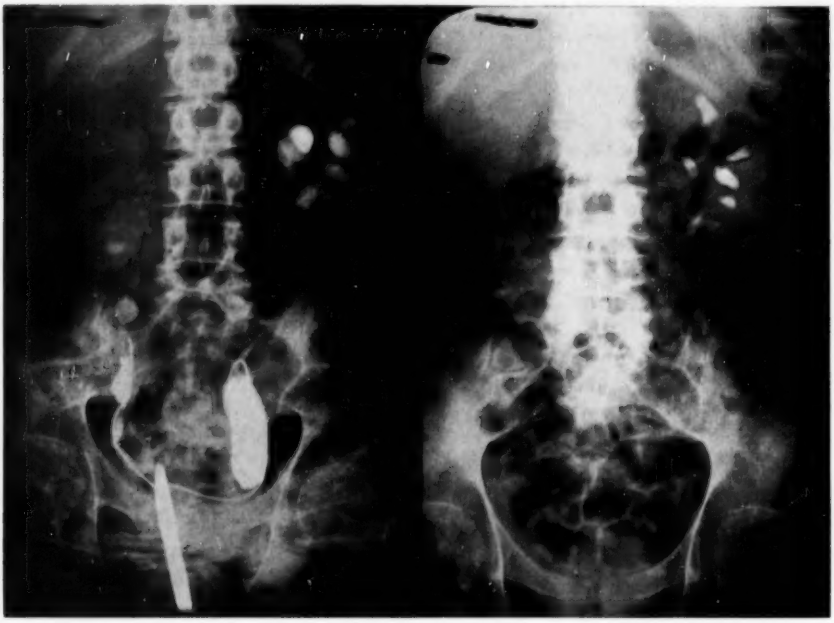

Figure 2

of the wire at the apex prevents the stone from impinging on the ureteral mucosa and rolling out of the basket as the stone is pulled toward the bladder. If there is great resistance as the stone is brought through the mural portion of the ureter, the orifice should be cut with a Collins knife and cutting current. If there has been much trauma by the manipulation, a catheter should be in the ureter for at least 48 hours. A bag catheter should be used to drain the bladder. The nurses and attendants should be instructed to irrigate the ureteral catheter, using isotonic sodium chloride solution, if obstruction and pain occur.

To prevent formation and to dissolve vesical calculi in bedridden patients, tidal irrigation [8] is effective except for oxalate stones.[8] At times reduction, or even dissolution, of stones in the ureter or kidney pelvis can be accomplished by automatic irrigation. The following case is illustrative.

A white man, 46 years old, had been a paraplegic for 12 years. During that time he had had two operations on the left side and three on the right side to remove calculi. One year before tidal irrigation was started, an extensive right perinephritic abscess had been drained. After that operation, the urinary drainage continued through the loin because of obstructing stones in the right ureter.

Cystoscopy revealed several vesical calculi, which were removed by litholapaxy. Neither ureter could be catheterized satisfactorily. The film (Fig. 2, left) shows three stones in the right ureter, several large stones in the left kidney, and a huge stone in the lower left ureter. A few days later a right ureterolithotomy was performed. A No. 14 F. rubber tube, which extended from the renal pelvis to the bladder, was left in the ureter 10 days. The drainage from the loin ceased.

Tidal irrigation of the bladder was then instituted, using 1 to 20,000 benzalkonium (Zephiran) chloride solution. The film (Fig. 2, right) was made after 15 days of irrigation. The stones in the left kidney had diminished in size, and the huge stone in the lower left ureter had disappeared. It seems reasonable to assume that the low surface tension of the benzalkonium chloride solution was a factor in the dissolution of these calculi.

POSTOPERATIVE TREATMENT

Postoperative abdominal distention is a frequent complication after open surgery on the kidney or ureter. Much suffering can be avoided if the patient swallows nothing until peristalsis is reestablished or passes gas by the bowel, or the bowels move.[9] While waiting for the return of peristalsis, the patient is given parenteral fluids. On the average, 2,000 cc. of 5% dextrose solution in water and 1,000 cc. of 5% dextrose in isotonic sodium chloride solution is used intravenously. After the establishment of active peristalsis, as heard through a stethoscope, food and fluid may be allowed unrestrictedly.

SUMMARY

The history of calculous disease is reviewed briefly. Some aspects are discussed regarding the preoperative examinations and indications for intervention. If a stone remains in the ureter indefinitely, irreversible damage to the kidney may occur without symptoms. A technique is described for removal of various types of calculus—open operation and cystoscopic manipulation. Two modifications are described to make the Johnson stone extractor effective. Experience has shown that prevention and dissolution of vesical calculi can be accomplished by tidal irrigation.

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CHRONIC EXTRADURAL HEMATOMAS

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THE ACCEPTED classic syndrome attending extradural hemorrhage is that of unconsciousness following injury, a lucid interval, a second period of unconsciousness, motor and sensory phenomena, and clear spinal fluid under increased pressure. This picture is thought by many authorities to arise only as a consequence of arterial bleeding which presents sufficient force to strip the dura from the internal surface of the calvarium to produce an acute, compressive, hemorrhagic tumor.

When this sequence of events is present in a person who has suffered a head injury, the diagnosis of an extradural hematoma is immediately obvious. That such a diagnosis is seldom so obvious is attested to by the presence of extradural hematomas in 12 to 20% of fatal head injuries.[1] In addition, during the past several years, reports have appeared suggesting that this so-called "classic progression" of disorders is the exception rather than the rule. In this regard, Brodin [3] reports the presence of a lucid interval in only 52.4% of his cases, while a typical lucid period was present in 35% of 23 subdural hematomas.

Two cases have recently come under our care, demonstrating a paucity of objective neurologic abnormalities, but with extensive, compressive extradural hemorrhage. The extreme deviation from the so-called "classic picture" of extradural hematoma, as seen in these patients, would seem to be worthy of report.

REPORT OF CASES

CASE 1.—R. D. C., a 30-year-old white man, was admitted to the hospital with the history that he had fallen, while intoxicated, from a moving auto trailer, on the night prior to admission. He was rendered unconscious by this fall and was said to have remained in an unconscious state for approximately 45 minutes. Following the injury, there had been some bleeding from the left ear, but at the time of admission, his only distress was that of persistent occipital headache.

Physical Examination.—The blood pressure was 134/82 and the pulse rate was 76 a minute. The patient was fully oriented, alert, and cooperative. The general physical examination was entirely negative. On neurological examination, the cranial nerves were quite normal in every

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respect, other than for a small amount of dried blood in the left auditory canal. No sensory or motor deficits could be found. The deep and superficial reflexes were normally active and symmetrical at all points. No pathological reflexes could be elicited.

Laboratory Findings.—The routine urine and blood studies were within normal limits. Cerebrospinal fluid was clear, under a pressure of 180 mm. of fluid, and contained 47 mg. of total protein per 100 cc. X-rays of the skull five days after injury revealed no evidence of fracture. The pineal body was calcified and in normal position. An electroencephalogram revealed focal delta activity in the region of the left temporal lobe, extending into the low frontal region (Fig. 1). Because of the absence of alpha suppression, this tracing was interpreted as being consistent with a cerebral contusion, rather than a space-consuming lesion.

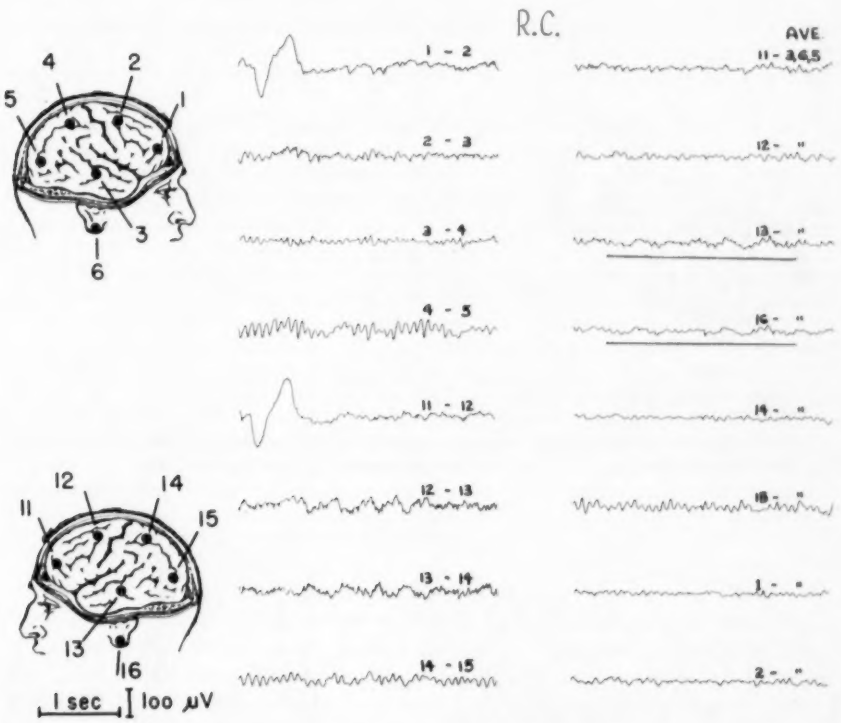

Fig. 1.—Electroencephalographic tracing in Case 1. The delta activity focal to the left temporal lobe is apparent. Both occipital leads, however, reveal a normal alpha pattern, with no suppression.

Hospital Course.—The patient continued to complain of occipital headaches, but the vital signs remained normal, and there was no alteration in the level of consciousness. Following lumbar puncture on the fifth day after injury, his headaches totally disappeared, only to return in severe form three days later. At this time, there appeared to be blurring of both optic disc margins, and positive Gordon and Oppenheim signs could be elicited bilaterally. Simultaneously, he developed a bradycardia of approximately 52 to 54. Because of these new developments, the skull x-rays were repeated, and the pineal body was at this time found to be shifted 5 mm. toward the right side. He was taken to surgery on the 11th day after injury, and a burr hole in the left parietal

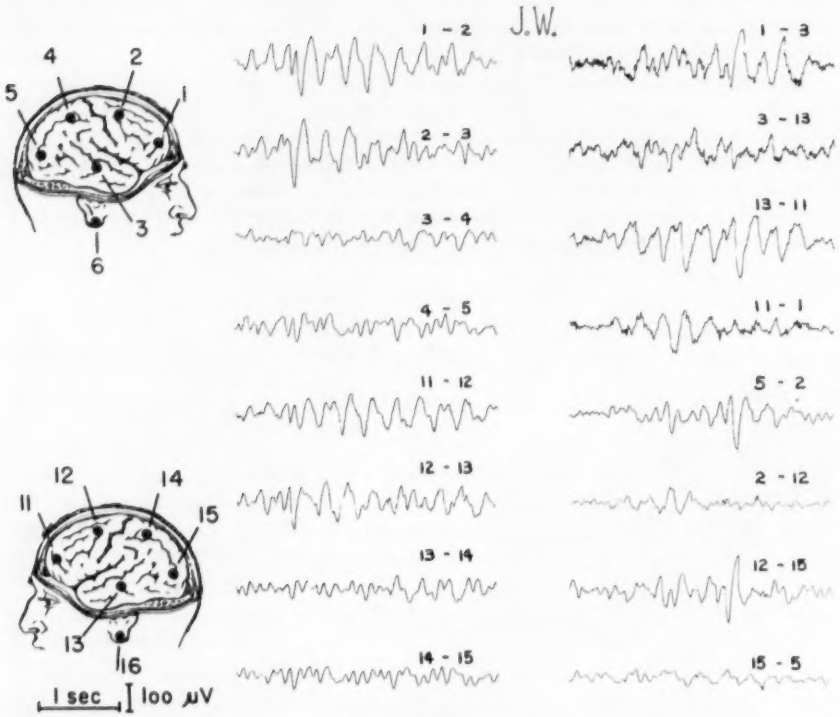

Fig. 2.—Electroencephalographic tracing in Case 2. The diffuse, slow dysrhythmia is apparent, and there is no suggestion of focal or hemispheric suppression of cortical activity.

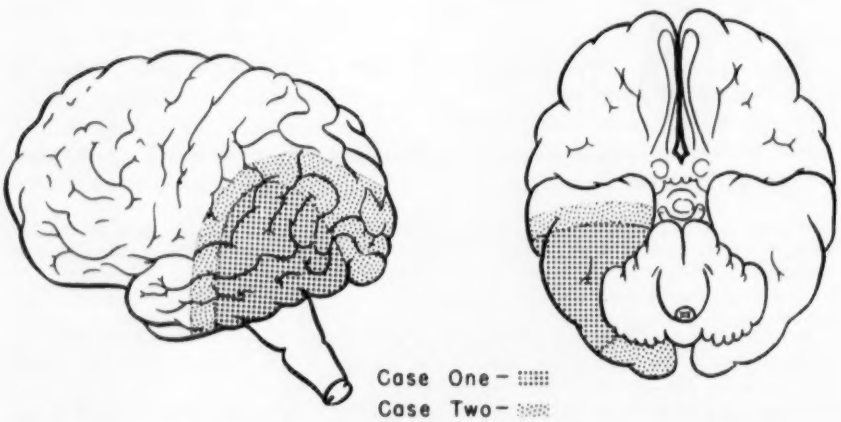

Fig. 3.—Diagram illustrating the position of the extradural hematomas as projected upon the surface of the brain.

region revealed a thick, extradural hematoma. This was exposed and evacuated through a parietal bone flap. The clot measured 2.3 cm. in thickness and extended onto the floor of the middle fossa (Fig. 3). The dura was tense and discolored, and when opened, there was found a small subdural hematoma extending over the parietal and occipital lobes. This was likewise evacuated. A small linear fracture was seen in the lateral portion of the petrous pyramid, but no active source of hemorrhage was found. The postoperative course was totally uneventful, and the patient appeared to have made a complete recovery when seen six weeks after operation.

CASE 2.—J. F. W., a 26-year-old white man, was injured in a fall from a motorcycle on the day prior to hospital admission. He was seen at an emergency hospital and was sent home. From the time of injury, he suffered severe supraorbital and occipital headaches. At the time of the accident he was rendered unconscious for approximately five minutes.

Physical Examination.—The blood pressure was 128/74, and the pulse rate was 60 a minute. The patient was alert and fully oriented in all spheres. He did not appear to be ill. The general physical examination was entirely negative. All cranial nerves were found to be within the limits of normal. No sensory deficits or motor weaknesses could be delineated. The superficial and deep reflexes were all hyperactive, but symmetrically so at all points. No pathological reflexes could be demonstrated.

Laboratory Findings.—The routine urine and blood studies were entirely normal. An electroencephalogram showed a diffuse, slow dysrhythmia, with no focal or hemispheric suppressions to suggest a discrete lesion. There were frequent bursts of bilaterally synchronous and symmetrical 2 to 4 cps waves. These were most pronounced in the frontal and precentral areas (Fig. 2).

Hospital Course.—During the early portion of hospitalization, the patient complained only of headaches. On the day after admission, during a severe headache, he vomited three times. Skull films at this time revealed a 5-mm. shift of the pineal toward the right side, but there was no radiographic evidence of fracture. On the third hospital day, repeat skull films revealed no change in the pineal displacement. At this time, the patient had developed a bradycardia between 45 and 52, but there was no hypertension, nor were there any reflex abnormalities or other neurologic change. A lumbar puncture revealed slightly blood-tinged fluid under 250 mm. of fluid pressure. On the fourth day after injury, the patient was taken to surgery where a trephine hole in the left parietal skull revealed a large extradural hematoma. This was exposed through a temporoparietal bone flap and was found to measure approximately 2 cm. in thickness. The clot extended downward to the floor of the middle fossa (Fig. 3). A small linear fracture of the temporal bone was seen at the time of surgery, but no active bleeding point could be demonstrated. After operation, the headaches were totally abolished, and when seen six weeks after surgery, the patient had no complaints of any kind.

COMMENT

In terms of the generally accepted clinical picture of extradural hemorrhage, it must be acknowledged that these patients were operated on during their "lucid interval." If this is so, then it is suggested that the early removal of the clots provided these patients with more assurance of complete recovery than if further delay had taken place. In this regard, it is noteworthy that the mortality with extradural hematomas is significantly less if the offending mass is removed prior to the appearance of depressed cerebral function.[2] In spite of the probability of delayed appearance of more serious signs, the question arises whether or not the clinical status of these patients might have improved, or remained static. Similar cases, with no greater deficit objectively, but with equal subjective distress, are called to mind in which a chronic picture of "post-traumatic" syndrome was followed for long periods without the benefit of trephine exploration. It has even been reported[3] that a parasagittal extradural hemorrhage has been observed to resorb spontaneously.

During recent years, there has been repeated reference in the literature to the isolated appearance of "chronic extradural hematomas." The longest period from

injury to operation known to be on record is the case reported by Grant [4] in which there was an interval of six years from the time of injury to operative removal of the hematoma. In this case, there was a heavily calcified membrane about the hematoma, attesting to its age. In the series of Munro and Maltby,[2] the average lucid interval was stated to be 3 days, the longest period of such a lucid state being 16 days. An interval of six weeks from onset to operation for extradural hemorrhage is similarly reported by Chambers,[5] who records another case in which the interval was two weeks. Similar cases have been reported by Olsen and Watson,[6] Brodin,[3] King and Chambers,[7] Jackson and Speakman,[8] Avol,[1] and Gurdjian.[9] This accumulation of data contradicts the belief, generally taught and accepted, that extradural hematomas are acute, rapidly progressing, hemorrhagic tumors.

The cases presented in this report are considered to fall into a category which could logically be termed "chronic extradural hematomas." In neither case would surgery have been undertaken without the evidence of pineal shift as divulged by the x-ray studies. No fracture was seen in the roentgenograms, and the patients presented none of the accepted signs classic for acute hemorrhagic compression of the brain. Since both patients were alert, fully oriented, and had no sensory or motor phenomena, the complaints could logically have been ascribed to cerebral edema secondary to trauma. It seems safe to suggest that the pineal displacement in both of these cases significantly reduced the patients' chances of suffering crippling residuals, or even death, since it was this abnormality that led to early surgical intervention.

The absence of motor and sensory phenomena is readily explained by the location of the clots in a region where motor or sensory cortex was not compromised. The lateral-basal position of the hematomas would also seem to explain the presence of pineal shift, since mechanical factors in this position would probably shift the pineal more readily than would a mass over the convexity, where extradural clots are usually found. In only 2 of the 14 cases of convexity extradural hematomas reported by Raaf [10] was there any displacement of the pineal.

The source of hemorrhage in these cases was not apparent, unless it was from the basilar fractures present. The position of the hematomas would suggest that this was the case. Wherever the origin of hemorrhage might have been, it can be assumed that it was a slow, low-tension, bleeding source. If so, the source also must be assumed to be venous, in spite of the fact that Vance [11] has insisted that an arterial laceration is always the origin of extradural hemorrhage. Slow venous bleeding could easily account for the delay in appearance of signs and symptoms beyond that seen when a meningeal artery is torn. A venous origin for the clot is further supported in Case 1, in which there was delayed appearance of pineal displacement. To our knowledge, a delay in the appearance of pineal shift has not previously been reported.

The absence of x-ray evidence of cranial fracture in these cases does not seem remarkable when it is noted that the basal area was primarily involved. Despite the fact that skull fracture usually attends extradural hematomas, it has been pointed out that it is not necessarily present with these lesions.* Moreover, Brodin,[3] has noted that in a series of 228 skull fractures, 61% were missed on roentgenographic

* References 3 and 10.

examination. Thus, failure to demonstrate a skull fracture radiographically should not be considered to eliminate the possibility of an extradural hematoma being present.

The electroencephalographic studies in these patients, although abnormal, failed to suggest the diagnosis. This is again understandable when the position of the hematomas is considered. The basal areas primarily involved are essentially unavailable for study by standard electroencephalographic technique. In addition to the fact that the involved cortical areas are distant from standard electrode placements, compression in this region would be expected to produce early, partial obstruction of the aqueduct, thus producing intracranial hypertension. The diffuse electrographic abnormality arising from this pressure would tend to mask any focal abnormality that might be present (Fig. 2). In the one patient in whom electroencephalographic localization was correct (Fig. 1), the etiology was ascribed to probable cerebral edema, since there was no attendant suppression of the alpha rhythm. It is doubtful if the electroencephalogram can be expected to suggest the presence of basal, compressive hematomas such as those here described.

The technical treatment of extradural hematomas is not attended by any monumental difficulty if the diagnosis can be made prior to irreversible damage to the brain. The two cases presented here, as well as a review of the recent medical literature, suggest that diagnosis of these lesions can be extremely difficult. Certainly, the current concept that the extradural hematoma is always an acute lesion is in need of revision.

SUMMARY

Two cases are reported in which there were large extradural hemorrhages manifested objectively by only a pineal shift. In one of these cases the pineal displacement arose slowly. We believe that these cases represent a clinical entity in the form of chronic extradural hemorrhage. In this regard, it appears that a venous source for such lesions is an actuality, and the long-standing requirement of arterial laceration for their production is in need of revision. These opinions are supported by multiple, similar, chronic, extradural hematomas reported in the literature. The failure to demonstrate a cranial fracture on x-ray does not prohibit the clinical suspicion of an extradural clot. From a clinical standpoint, the presence of such a lesion may be unattended by any detectable, objective, neurologic deficit. The electroencephalogram may be of no aid in reaching an accurate diagnosis and may even be misleading.

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INTERSTITIAL CYSTITIS

An Adjunct in Its Treatment

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DETROIT

IT WAS just 50 years ago that Nitze [1] described "cystitis parenchymatosa" in the German literature. The attention of the American physician was not focused on this entity until 10 years later. At that time, Hunner,[2] unsatisfied with the "waste-basket" diagnosis of "neurotic bladder," aptly observed and presented the clinical and pathological features of interstitial cystitis much as we know them today.

He described interstitial cystitis as a disease with a primary predilection for the female, as did others, and subsequent reports have cited its presence occasionally in the male. It begins insidiously in the third decade of life. By the fourth to the sixth decade the syndrome is at its height, adding wretchedness to the already nervous, uncertain, and depressed menopausal woman.

Clinically, interstitial cystitis is characterized by the triad of clock-like frequency, both day and night, suprapubic pain, and, usually, a sparkling, clear urine. Its course is chronic and progressive, terminating in almost continual pain and urgency. These symptoms are the result of gradual fibrosis and contraction of the bladder. Occasionally, ureteral reflux and hydronephrosis accompany the diminished vesical capacity.

Microscopically, the initial lesion occurs in the submucosa. Patchy areas of fibrosis and round cell infiltration in this layer eventually become confluent and diffuse, extending through the muscularis to the serosal surface. Around these lesions there is marked vascular proliferation and venous and lymphatic distention. Mucosal changes are minimal and may consist of only slight "blanching" on distention, or pinpoint ulcerations. The ease with which these lesions may be missed cystoscopically led Cullen to name them "elusive ulcers."

The similarity of these pathological changes to chronic inflammation elsewhere in the body and the frequency with which these patients were noted to have sterile urine cultures led Hunner [2] initially, and Meissner and Bidgood * and Seaman [5] after him, to the conclusion that they were secondary to "foci of infection." Bumpus [6] and Hinman [7] suggested that the lesions were due to a "streptococcus with an affinity for the urinary tract." The advent of antibiotics has not diminished the incidence or increased the cure rate in this disease. The results so obtained have not warranted its continuation.

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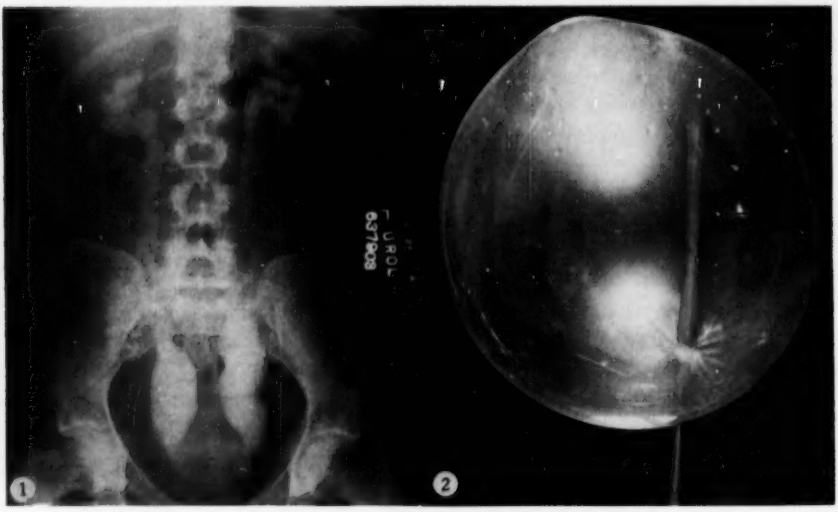
* References 3 and 4.

Van Duzen and Rhoads,[8] noting the severe vesical fibrosis, suggested the use of alpha-tocopherol. Vitamin E had, after all, been somewhat effective in certain cases of fibrositis and in Peyronie's disease. The results did not warrant the continuation of such treatment. More recently, Paquin and Marshall [9] and Dees,[10] suspecting a relationship to collagen-like diseases, have employed corticotropin (ACTH) and cortisone, with some success.

More thought-provoking, however, are the pathological findings of Hand.[11] This observer noted that, in addition to the marked fibrosis, there occurred large accumulations of inflammatory cells both in and around nerve bundles in the bladder wall. He suggested that perhaps the disease is of neurological origin. His description is faintly reminiscent of the round cell cuffing and infiltration and gliosis seen in numerous central nervous system diseases. The predominance of pain in



the disease syndrome lends some credence to this hypothesis. Nesbit's report [12] of a cure following anterolateral chordotomy in an advanced case arouses one's speculative curiosity. Is there a virus with a predilection for intramural vesical nerve tissue?

From these comments, it is obvious that the pathogenesis of interstitial cystitis is unknown. Hunner [13] himself, in an address some 16 years after the publication of his original article, had nothing to add. Treatment has thus remained symptomatic and empirical, and hence rarely curative.

The use of the varied conservative measures in the early stages of the disease is common knowledge. Instillations, irrigations, the use of varied vesical analgesics, the transurethral submucosal infiltration of absolute alcohol or procaine, periodic hydraulic distention, with or without fulguration, and the topical application of silver nitrate are all familiar palliatives in the urologist's armamentarium.

In the advanced stages of the disease, the surgeon may offer the patient cystectomy, total or partial, with the choice of ureterocutaneous or ureterosigmoid transplants. Folsom [14] has offered these unfortunate people more hope. He has

reported seven cases of subtotal cystectomy after which complete regeneration of the bladder, with a near-normal capacity, occurred. For those whose pain is intractable, presacral neurectomy, sympathectomy, and anterolateral chordotomy have been advocated.

What of the patient with contracted bladder unwilling to accept surgery? Of late we have seen several such patients. Not infrequently they have marked stenosis of the ureteral orifices, unilateral or bilateral reflux (Fig. 1) hydroureter, and hydronephrosis. Despite vesical capacities in the neighborhood of 30 cc., these patients have obtained temporary, though progressively diminishing, relief from periodic hydraulic distention. Most certainly such a procedure in the presence of reflux makes eventual upper tract infection a distinct likelihood.

It is the duty of the urological surgeon to conserve renal tissue and function as much as it is to give symptomatic relief. With the aid of the Ford Motor Company

Research Engineering Laboratory, we have developed a small device, simple in structure, the use of which, we believe, diminishes the probability of upper tract infection in patients with severely contracted bladders undergoing periodic hydraulic distention.

The device consists of an 18 F. whistle tip straight rubber catheter, to the end of which is attached a distensible 1/5,000-in.-thick condom-type rubber bag. The bag has a capacity of 1,000 cc. (Fig. 2), so that the danger of rupture is minimal and reflux of the distending medium nonexistent.

Using sterile precautions, the catheter bag is inserted into the empty bladder. The bag is then gradually distended with water until the desired capacity is reached (Fig. 3).

In none of the patients with reflux so treated has there been evidence of upper tract infection following distention. The use of this device certainly seems indicated to prevent further complications in these already wretched and unhappy people.

SUMMARY

The history of interstitial cystitis is briefly reviewed.

The use of a catheter-bag device for periodic distention in patients with contracted bladder and ureteral reflux is suggested, in order to minimize upper tract infection, when more radical and definitive surgical measures are contraindicated or are refused by the patient.

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AVULSION OF THE SCALP

Report of a Case with Ten-Year Follow-Up

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FORTUNATELY, in the annals of medical history there are few recorded cases of complete avulsion of the scalp. Years ago, the Indians were noted for their characteristic treatment of the white man, as well as strange tribesmen. One of the most amazing descriptions of scalp injury was reported by Howard and his associates,[2] which concerned a 61-year-old rancher in Montana who received mutilating injuries from a grizzly bear. There was loss of the entire scalp and pericranium. The patient, surprisingly, survived the ordeal. In the past, when there were less strict regulations influencing the rate of industrial accidents, many types of injuries were encountered. Avulsion of the scalp was possibly commoner then than at present. No one physician or surgeon has had the opportunity of treating a large series of these cases; hence, it seems worth while to report the case of a woman factory worker first treated 10 years ago who was re-examined recently.

REPORT OF A CASE

On Aug. 13, 1943, Mrs. L. K., 33 years, was admitted by ambulance to the emergency room of the Presbyterian Hospital, Chicago, on the service of my father, the late Carl B. Davis. She stated that as she was loading a 12-ft. bar into a screw machine, she felt her hair catch and spin on the rod. The next instant she placed her hand to her head and felt that "all of her hair was gone." Her hand was covered with blood. No loss of consciousness was experienced. Pain was described only as a "feeling of soreness." A pressure dressing had been applied to the head by the company physician. The patient was rushed immediately to the operating room for surgical treatment.

The admission physical examination revealed a young woman who was emotionally upset but whose general condition was satisfactory. When the bandage was removed, a large percentage of the scalp was found to be missing. A thin aponeurotic layer covered the calvarium The avulsed tissue extended from the frontal hair line to the occiput, where there was a short dangling flap. Laterally on the right, the temporal area was completely denuded, while on the left there was a flap of scalp hanging down over the ear. There was marked edema and subsequent ecchymosis of both upper eyelids.

A few active vessels were secured immediately with sterile hemostats. Ethylene anesthesia was administered. All remaining hair was shaved away. Dirt and grease were removed with solvents. The denuded area was thoroughly cleansed with a nonirritating soap and irrigated with isotonic sodium chloride solution. The scalp edges were débrided. Over the right occiput, the soft tissues were reapproximated. Sulfanilamide powder was sprinkled over the raw surface. A sterile petrolatum pressure dressing was applied. Consideration was given to the application of split-thickness skin grafts, but because of the risk of infection and possible failure of the

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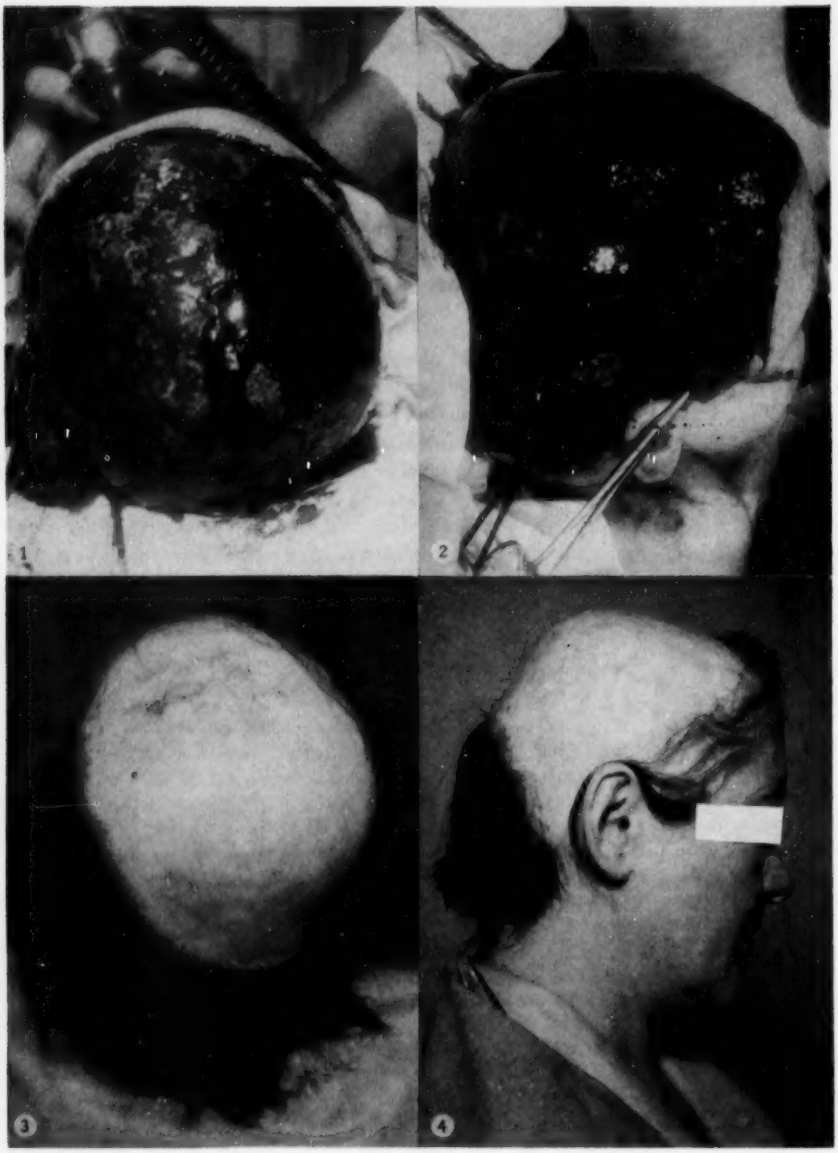

Fig. 1.—Appearance of the periosteum prior to any definitive treatment. Note the flap of scalp hanging over the left ear.

Fig. 2.—Lateral view of the head, showing the extensive loss of scalp over the right temporal area. Observe the flap of scalp in the occipital region and the hemostats applied to active arteries.

Fig. 3.—Photograph demonstrating the extent of loss of scalp. There is an area of macerated skin to the left of the vertex. On the occiput numerous elevated regions are seen, representing the original pinch grafts.

Fig. 4.—Right lateral view, showing the extensive loss of scalp over the temporal area.

Fig. 5.—Left lateral view, showing the segment of scalp, which, although torn loose at the time of the injury, bears hair in abundance.

Fig. 6.—Patient at present, with transformation: *A*, anterior view; *B*, lateral view.

grafts, additional definitive surgery was postponed. Transfusions of whole blood and dextrose solution were administered. Sulfathiazole was given parenterally. Tetanus antitoxin, 1,500 units, was given, without reaction.

On Sept. 1, 1943, approximately 16 days after admission, after a low-grade infection (Staphylococcus aureus) had been controlled, 25 to 30 pinch grafts from the thigh were applied about 1 in. (2.5 cm.) apart to healthy granulations. Fine-mesh petrolatum gauze was placed over the grafts. A pressure bandage completed the head dressing. On Oct. 8, three strips of split-thickness grafts were used to cover a raw surface over the occiput. From time to time warm moist dressings of boric acid solution were used to clean up small areas of infection. The open-air treatment proved to be beneficial late in the care of this wound.

For many weeks the patient complained of headaches and visual disturbances. Repeated eye examinations revealed no pathology to account for the symptoms. Blood pressure readings were normal constantly. Neuralgia of the face was present for many weeks, before it finally disappeared. On Jan. 28, 1944, four and one-half months after the injury, the patient was discharged from the hospital, still receiving treatment to a few resistant scalp areas, which seemed to break down at intervals.

The patient was not seen again as she returned to her own physician, until the fall of 1953, when, by special request, she came to the outpatient department of the hospital. She stated that she was well and that while wearing a transformation, nobody except her close friends were aware of her previous injury. She seemed pleased about the end-result. Two children had been born since the accident. Her only complaint was that during warm weather maceration of the skin developed over the vertex. In 10 years no sensation had returned in the injured area.

COMMENT

In 1911, Davis [1] outlined some of the fundamental principles in the treatment of avulsion of the scalp and reviewed all cases reported up to that time. Since then numerous reports in the literature have dealt with an isolated incident of total or partial avulsion; yet no one author has had experience with a large number of such cases. Instead of employing free skin grafts, some of the early authors advocated the use of pedunculated or tubed pedicle flaps in closure of the defect. McWilliams [4] stated that up to 1924 "there have been 173 instances of total avulsion of the scalp in the literature, with fourteen (eight per cent) deaths. The scalp was replaced in forty patients and in not a single instance did the replaced scalp survive. Only a partially avulsed scalp with a pedicle may be replaced." It is interesting to note that 30 years ago, he wrote as follows:

> The most efficient method of treating this severe lesion, provided the patient is treated within 24 hours of the accident, is to sterilize the raw skull and, at the same time, drill holes in the diploe in that part of the skull that is bare of all soft parts so as to hasten its granulation, then to shave the avulsed scalp, saving the hair for a future wig; to take Thiersch grafts from its surface at once, and to transplant these grafts to the denuded, raw skull area.

In 1935, Otto [6] described the case of a woman factory worker who caught her hair in the wringer of an electric washing machine. An extensive area of the scalp covering only the crown of the head had been avulsed. He recommended that in this case, as well as in many cases of extensive avulsion of the scalp, the defect may be treated successfully without grafting because the scalp has moderate mobility and elasticity, permitting marked stretching. He advocated that multiple closures may be done without distortion of the face or ears. He emphasized that the abundant blood supply of the scalp will permit marked suture tension without slough.

In 1946, Kazanjian and Webster [3] reviewed the literature on this subject and, in an excellent study of the problem, emphasized that split-thickness grafts could be

applied immediately to the exposed periosteum. In addition, Osborne [5] cited Geinitz and Erhardt as early workers who employed Thiersch grafts from the avulsed scalp for reconstruction of the defect.

In 1950, as the result of experimental work on thin or split-split grafts bearing normal hair on the pig, Osborne recommended the clinical application of the experimental method with the human scalp. An interesting case is reported in which such grafts were used immediately from the scalp for coverage of a defect produced by wide surgical excision of a scalp neoplasm. Another case is described in which immediate split-thickness grafts were taken from the avulsed scalp itself. Geinitz recommended tacking an avulsed scalp to the wooden head of a milliner's mannequin and cutting Thiersch grafts from it with a razor type of grafting knife.

When complete avulsion occurs, attempts to replace separated scalp have resulted invariably in failure. In 1946, Straith and McEwitt [7] demonstrated with excellent colored illustrations the appearance of the necrotic scalp (18 days after avulsion) which had been replaced earlier by an industrial surgeon. The dead scalp tissue was removed, and subsequent clean granulations were covered by split-thickness dermatome grafts, held tightly in place by fibrin fixation through the use of thrombin solution and plasma. These authors emphasized that this method enhances the probability of successful takes and provides an excellent method of fixation.

In 1951, Wynn [9] reported a case of total scalp avulsion and emphasized that the surgeon must provide adequate skin coverage in a minimum period. He advocated the use of a predetermined pattern of a scalp defect, which gives the surgeon an idea of the amount of skin needed, and then recommended suturing the skin grafts together before actual application to the head wound.

If only portions of periosteum have been lifted up as flaps, they should be sutured back in place. Ample experience has demonstrated that the periosteum is vascular enough to sustain skin grafts. Although the earlier physicians felt that skin grafting should be postponed until granulations had formed on the periosteum, modern surgeons hasten to close the wound before granulations appear. Osborne emphasized that the "best reconstruction time after scalp avulsion is a short-lived one and does not return." However, in our case, with extensive avulsion of the scalp and apparent contamination of the wound, it seemed proper to postpone grafting until the danger of infection had passed.

In instances in which there is loss of the entire scalp, including periosteum, numerous authors have recommended multiple drill holes through the outer table of the skull, with the subsequent development of the growth of granulations to which skin grafts may be applied later. Strayer [8] reviewed the history of this surgical procedure and related that as far as could be determined, the origin of this technique goes back to Augustin Belloste in 1696. Kazanjian and Webster found that in instances in which there is loss of periosteum, a method for obtaining a vascular bed for grafts is best accomplished by chiseling away the outer cortex until multiple bleeding points appear. In a week or so, the granulations now present are grafted. However, experience has taught that in some cases skin grafts immediately applied to the exposed cancellous bone have taken well; consequently, thin grafts so placed on freshened bone may be employed.

CONCLUSION

A case of extensive avulsion of the scalp is reported in a woman factory worker who was treated 10 years ago. The treatment consisted of early cleansing and débridement of the wound, with secondary application of multiple pinch grafts and subsequent split-thickness grafts. Secondary infection developed during the course of treatment. Sulfathiazole was used parenterally, as the present-day antibiotics were not available at that time. Some maceration of the new scalp occurs in warm weather. The patient has lived a normal life since the accident.

Immediate application of split-thickness grafts to the periosteum might have resulted in an earlier closure of the wound and shorter hospitalization. However, the wound was considered to be contaminated and potentially infected so that immediate coverage by grafting was postponed.

Every effort should be made in the shortest period of time to convert an open wound into a closed wound by the early application of split thickness skin grafts, provided the operative wound is clean. As the result of the experience of recent authors, this treatment is considered to be the one of choice in cases of complete avulsion.

If there is loss of periosteum, a suitable surface may be prepared for the application of skin grafts by drilling holes in the outer table or by chiseling away the outer cortex. The use of split-thickness grafts obtained by the Padgett dermatome from the human scalp is advocated by some. As the result of experiments on the pig, Osborne has applied successfully split-split grafts which bear normal hair. This treatment designed to secure normal hair is intriguing and should prove of value in cases of this type.

It must be emphasized that there is great tendency to replace the avulsed scalp, but previous experience has proved the futility of this procedure. The avulsed scalp may be saved to obtain skin grafts for coverage or to preserve the hair for a transformation or wig.

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NASOPHARYNGEAL CARCINOMA

I. Clinical Analysis of One Hundred Twenty Cases

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THE HIGH incidence of nasopharyngeal tumors among the Chinese has been noted by many observers. In Singapore, a colony which has a cosmopolitan population, but in which the majority are people of Chinese race, the opportunity is afforded to study these tumors and to compare their relative incidence in different ethnic groups. The problems raised in a study of this condition are numerous, and for many years research work has been undertaken on various aspects. It is proposed to carry out a series of studies collating previous findings with more recent research and to approach the problem from different aspects. The first paper contains an analysis of the clinical findings.

One hundred twenty cases of nasopharyngeal tumors seen in the General Hospital, Singapore, during the years 1947 to 1953, have been studied; 46 patients were seen at first hand, and the remaining information was obtained from the case records. For convenience, we have used the term "lympho-epithelioma" to designate this group of tumors, but it is recognized that the histogenesis and character of these neoplasms are highly controversial and the use of the term is open to criticism. The pathological study of our cases is as yet incomplete and will form the basis of a later paper. In general, these tumors show the picture of an undifferentiated epithelial neoplasm with considerable lymphocytic infiltration corresponding to the description given by Cappell (1934). While the diagnosis "lympho-epithelioma" has been confirmed histologically in every instance, this analysis has been made essentially on a clinical and not on a pathological basis.

ETHNIC GROUPS

Bonne (1937) has observed that cancer does not behave in the same way in different races of mankind. He considers that the high incidence of malignant tumors of the lymph nodes of the neck would seem to be peculiar to the tropical countries of the Far East, and although he is not convinced that the nasopharyngeal tumor is necessarily the primary growth, there is a striking similarity between the tumors he describes and those in this series. Nasopharyngeal carcinoma has been quoted by Mekie as the third commonest type of cancer in Singapore and by Digby as the second commonest type in Hong Kong. Digby (1941) recorded 210 cases occurring in Chinese and stated that while he had also seen the disease in Filipinos and Indians, he had never met it in a European.

While nasopharyngeal carcinoma has been described in persons of the white races by several authors, the number of cases in any one series has usually been small. The fullest description of a large number of cases has been given by Simmons and Ariel (1949), writing from Illinois, who described 150 cases seen over a 16-year period. Of these 150 patients 88% were white, 11.3% Negro, and 0.6% (1 patient) Chinese, but these percentages did not differ significantly from the number of persons of each race admitted to the hospital. Godtfredsen (1947), in a paper dealing with the ophthalmic-neurological symptoms of the disease, has collected 454 cases from the Scandinavian radiological clinics over a 10-year period. He states that nasopharyngeal carcinoma constitutes 0.4% of all cases of cancer occurring in Scandinavia. This makes an interesting comparison with corresponding figures obtained in Singapore (Mekie, 1949) and Hong Kong (Digby), which were 16.41% and 27.2% respectively.

In the present series, all but one of the patients were Chinese, the exception being a Tamil.

TABLE 1.—*Chinese Ethnic Groups*

Ethnic Group	Present Series		Population of Colony of Singapore (1947 Census)
	Total No.	% Total Chinese	% Total Chinese
Cantonese	34	28.6	21.6
Hokkien	33	27.7	39.6
Hailam	18	15.1	7.2
Khek	12	10.1	5.5
Teochew	17	14.3	21.5
Other Chinese	5	4.2	4.6

TABLE 2.—*Age Distribution*

Age, Yr.	Patients, No.		Males		Females	
	Total	%	Total	%	Total	%
Under 20	2	1.7	1	1.1	1	3.3
20-29	14	11.8	9	10.1	5	16.7
30-39	34	28.6	25	28.1	9	30
40 and over	69	57.9	54	60.7	15	50

It is interesting to note that of the Chinese, the percentage of Hailam and Khek patients was significantly higher than the general population of Singapore (1947 Census), while that of Hokkien and Teochew was considerably lower.

AGE AND SEX

The average age was high, more than half (69) of the patients being over 40 years old on the first observation. The disease tended to occur slightly earlier in women, as Digby found in Hong Kong, although in his series, the greatest number of cases in both sexes occurred between 31 and 40 years.

The sex incidence showed a predominance of males in the ratio of 3:1 as compared to the male-female ratio of the general population which is 1.13:1. Digby gave the sex incidence as 3.2 men to 1 woman.

There was nothing to indicate that any particular trade or occupation predisposed to the condition.

DURATION

On first presentation of the patient at the hospital, the duration of disease varied from one month to seven years, the average time being one year. There was no constant relation between the length of illness and the severity of symptoms.

SIGNS AND SYMPTOMS

It is not necessary to enlarge upon the very full description which Digby has already given. Here it is our intention mainly to indicate the frequency of each sign and symptom of the disease in this series.

Initial Complaint.—The initial complaint was most commonly enlargement of the cervical lymph nodes. Epistaxis, headache, and, less frequently, deafness, tinnitus, nasal obstruction, diplopia, and blurring of vision also occurred as the earliest symptom in some cases.

TABLE 3.—*Initial Symptom*

Initial Symptom	No. Patients
1. Cervical adenopathy	83
2. Epistaxis	18
3. Headache	15
4. Disturbance of hearing	6
5. Nasal obstruction	5
6. Visual defects	4

In some cases, several symptoms appeared simultaneously; in particular, epistaxis and nasal obstruction occurred together in four instances.

The cervical lymph nodes were enlarged in 108 cases, and this occurred as an early feature of the disease. Adenopathy was found to be bilateral in 58 patients and unilateral in 50 when the patients came to hospital. Typically, swelling first appeared below and behind the angle of the mandible, and this gradually extended to involve the other deep cervical lymph nodes. In many cases, enlarged nodes were palpable along the sternomastoid as far as the clavicle, in the supraclavicular region, and along the upper border of the trapezius.

The axillary lymph nodes were involved in only four cases (Fig. 1).

Primary Growth.—This was detected in 75 patients and was accompanied by glandular enlargement in all but 11. In 8 of these 11, there were cranial nerve lesions and radiological evidence of cranial bone involvement. Of the 64 with glandular metastasis, 28 had cranial nerve lesions, and only 11 showed extension into the skull on x-ray. It would seem, therefore, that tumors which do not metastasize to the cervical lymph nodes are more likely to spread upward and to involve the cranial nerves.

The primary nasopharyngeal tumors were found to fall into the two main classes which Mekie has already described: (1) the small slightly-raised, hard plaque which ulcerates early, and (2) the fungating, exophytic type of growth. Patients with a growth of the first kind gave on the average a history of six months longer duration than did those with the second type. In only 50 cases was the tumor described adequately enough to enable this classification to be made; 21 of these 50 fell into the first group, and 29 were exophytic. It is interesting to note that while 20 patients

Fig. 1 (left).—Man, aged 35, with enlargement of the axillary lymph nodes following radiotherapy.

Fig. 2 (right).—Man aged 48, with three-year history; presented with a small degree of cervical adenopathy, small ulcerating tumor in nasopharynx and lesions of right cranial nerves III, V, VI, and XII.

Fig. 3 (left).—Girl of 26, with fungating nasopharyngeal tumor and enlarged cervical lymph nodes on left side.

Fig. 4 (right).—Same girl as in Figure 3, showing enlarged cervical lymph node.

with a small ulcerating lesion in the nasopharynx showed cervical adenopathy, this feature was exhibited by only 21 with the second type of tumor. The glandular enlargement, however, was much grosser in the second group than in the first. There was no appreciable difference in the number of either group with cranial nerve lesions or in the radiological findings. In both types when the cervical lymph nodes were involved late in the disease, there was early and often multiple cranial nerve damage (Figs. 2, 3, and 4).

The site of origin of the growth was located in only 31 cases either by personal observation or in the case records and was most commonly the lateral wall of the nasopharynx in the fossa of Rosenmüller and around the orifice of the Eustachian tube. Tumors were also found to arise from the posterior wall, and, less commonly, from the roof and the tonsil.

The Main Symptoms.—Epistaxis, nasal obstruction, headache, deafness, tinnitus, chronic aural discharge, visual disturbances, numbness or neuralgia of the face, trismus, and dysphagia were the main symptoms.

TABLE 4.—*Origin of Primary Tumor*

Site	Total No.	Small Ulcerating Type	Fungating Type
Lateral wall	14	5	9
Posterior wall	9	5	4
Roof	5	3	2
Tonsil	3	1	2

TABLE 5.—*Cranial Nerve Lesions*

Order of frequency	1	2	3	4	5	6	7	8	9	10	11
Nerve	VI	XII	III V	VII	II	IX	IV	X	XI	VIII	I
Total no.	31	19	16	12	11	10	8	7	6	5	3

A large number of patients were first seen at the Ear, Nose and Throat Department; 58 patients (48.3%) had epistaxis which in 33 cases was associated with nasal obstruction, the latter occurring alone in 10 instances. Of the 46 patients seen personally, however, 30 exhibited epistaxis as a symptom. These symptoms were neither essentially an early nor a late feature of the disease, but in very few cases did epistaxis persist for longer than six months before a doctor was consulted.

In 75 cases (62.5%), headache was a symptom and in many instances, by far the most distressing one. The pain was usually situated in the temporal region, and, less frequently, occipital or generalized. When the site of headache was the temple, it was usually unilateral.

Symptoms related to the ear, of which unilateral deafness was most frequent, occurred in 51 patients (42.5%). Tinnitus commonly accompanied the deafness, which often became bilateral late in the disease and was in many cases associated with a chronic discharge from the ear. The deafness appeared to be due to blockage of the Eustachian tube rather than to a lesion of the eighth-nerve.

Fifty-four patients (45%) exhibited cranial nerve lesions, multiple ones in 35 instances. When one nerve only was affected, this was most frequently the sixth

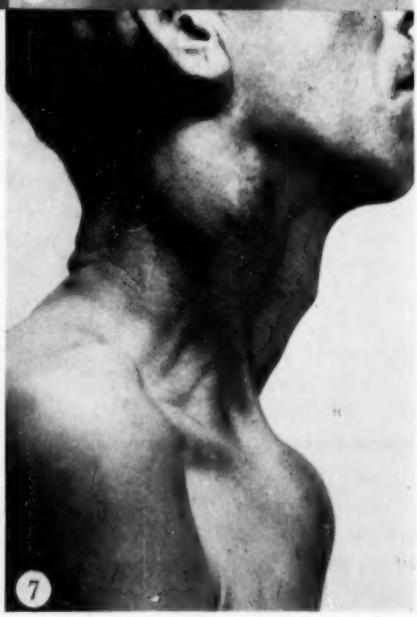

Fig. 5.—Multiple cranial nerve lesions in man of 38, with 18 months' history. On left, only nerves VIII and XI were intact. On right, there are lesions of nerves II and III. There is marked proptosis and conjunctivitis of left eye.

Fig. 6.—Man of 45, with two-year history; bilateral cervical adenopathy, massive on right; fungating nasopharyngeal growth, no cranial nerve lesions, and secondary deposits in sternum.

Fig. 7.—Side view of same patient as in Figure 6, showing massive cervical adenopathy.

(seven cases). Single nerves were affected in all 54 cases in the following order: The commonest combination of nerve lesions was III, IV and VI, while VI and XII were together involved in several cases, and lesions of IX, X, and XI also occurred fairly frequently (Fig. 5).

Symptomatically, while diplopia and failing sight, numbness or pain in the face, and dysphagia were frequently stressed by the patient, few volunteered a complaint of squint until specifically questioned.

Radiological evidence of cranial bone destruction by tumor was found in 30 of the 54 patients with cranial nerve lesions, and in 18 cases in which examination of the cranial nerves revealed no abnormality. Erosion of the floor of the middle cranial fossa and the sella turcica and opacity of the sphenoidal sinus were common signs of cranial involvement. In only three cases was the vault of the skull affected, and distant metastases had already occurred to other bones in each case.

A soft tissue swelling in the nasopharynx was a frequent radiological finding, and in several cases this was demonstrable before any lesion could be seen on clinical examination of the nasopharynx.

Distant Metastases.—On 17 occasions distant metastases occurred, this finding being confirmed either by x-ray or at autopsy. Deposits were most frequently found in bone (13), the spine, ribs, femur, pelvis, clavicle, and sternum, being involved in that order. Three cases had pulmonary metastases, and one only had secondary metastases in the liver and spleen. This distant spread was always a late feature of the disease, and usually occurred after radiotherapy.

PROGRESS

Follow-up investigation has not been fully carried out until the last year. In all, 23 patients (19.2%) are known definitely to be dead. Since February, 1953, of 46 patients seen, 17 (37%) are known to be alive, the longest duration of life since the earliest symptoms being 3 years, and the average duration 13½ months. Ten people have died, and another 10 who attended the clinic regularly and then failed to return are presumed dead. The nine remaining patients either live too far away to report as outpatients or have failed to come back at all since discharge from hospital.

It has not been possible to ascertain the immediate cause of death in every instance, and in the case of three patients who died at home, no information is available. Prefrontal leucotomy was performed in some patients with advanced disease and intractable headache, and in five instances the patient died within a week of operation. Three others with extensive cranial nerve lesions and erosion of the skull were found to have softening of the temporal lobe with hemorrhage at postmortem examination. One man had a metastasis at the cerebropontine angle, which gave rise to sudden collapse, hyperpyrexia, and death. Five patients died of respiratory obstruction due to secondary deposits which were obstructing the air passage. Two had terminal pericarditis, and three more had widespread metastases, including deposits in the lung.

SUMMARY

One hundred twenty cases of nasopharyngeal carcinomas occurring over a six-year period have been reviewed with regard to race, age, sex, duration of symptoms, type and site of primary growth, symptomatology, and progress.

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MASSIVE BLEEDING FROM COMMON BILE DUCT CAUSED BY INDWELLING T-TUBE

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THE DEVELOPMENT of hemorrhage in the common bile duct consequent to an indwelling T-tube is one of the more serious complications of biliary surgery. Though rare, it is of importance to surgeons because it is a distressing and dangerous condition which can be combated at times only by surgical measures. A review of the literature reveals the infrequency with which this condition has been observed and reported. Its chief interest, however, lies not in its relative infrequency but in the mechanism of its formation and the dire consequences which may follow this condition if left unrecognized and untreated.

Our interest in this subject was aroused by two cases with massive bleeding from the common bile duct attributed solely to the presence of an indwelling T-tube within the duct. The bleeding in each instance was detected soon after the blood found its way through the tube to the outside. We believe the condition is sufficiently uncommon to warrant a record of the cases which we met in our practice. No doubt, not all such cases are reported, but some idea of the infrequency of this condition could be discerned from the fact that throughout our entire surgical career we have observed only two such cases. This article contains an account of the clinical picture of this condition and is presented mainly in the hope that delays in recognition and treatment may be prevented.

REPORT OF CASES

CASE 1.—M. T., a 41-year-old man, was admitted to the Brooklyn Jewish Hospital complaining of intermittent attacks of acute abdominal pain of several years' duration. The most recent attack occurred three days before his entering the hospital and consisted of sharp, colicky pain in the right upper abdomen. The pain radiated across the back and to the right shoulder. The patient also noted for the first time that his eyes were turning yellow.

The physical findings on admission to the hospital were briefly as follows: The patient was well developed and well nourished, with a definite icterus of the skin. The heart and lungs were normal; blood pressure was 130/75. The abdomen was soft and free from tenderness or spasticity; the gall bladder could not be palpated.

Laboratory Data.—The urine was of a deep dark-brown color and contained free bile. The red blood cells numbered 4,200,000; the white blood cells, 9,500 and hemoglobin was 90%. A cholecystogram obtained on a previous occasion outside the hospital revealed a nonfunctioning gall bladder and multiple stones within its lumen.

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At operation, the peritoneal cavity was opened through an upper right rectus incision. The gall bladder was enlarged; its wall was thickened and edematous, and the lumen contained multiple small calculi. The common bile duct was not very dilated, and palpation of its wall through the foramen of Winslow failed to disclose the presence of stones within its lumen. However, because of the existing jaundice, the duct was opened and explored. A few small calculi were found obstructing the distal end of the duct and were removed. After this a soft rubber catheter passed readily through the duct into the duodenum; also, when the catheter was irrigated with isotonic sodium chloride solution, the duodenum was found to distend with fluid, thus indicating that the obstruction in the duct had been relieved. A soft rubber T-tube with short side-arms was then inserted into the common bile duct through the exploratory incision made in its anterior wall, and the abdominal wall was closed in layers.

The patient did well after the operation. A cholangiographic examination done on the eighth postoperative day disclosed the presence of two rounded shadows in the distal end of the common bile duct, suggestive of calculi. In view of this disclosure, the T-tube was not removed as intended and was left in situ. On the 10th postoperative day the patient suddenly noted a profuse flow of blood escaping through the T-tube. He soon became weak, anxious, and cold; the pulse was rapid, and he presented a picture of internal hemorrhage. The patient was given an immediate transfusion of 500 cc. of blood, after which he rallied and the bleeding was less profuse. The ductal bleeding was attributed to an erosion of a blood vessel caused by the continuous irritation of the indwelling rubber tube, and it was therefore removed. This was followed by rapid and complete cessation of bleeding. Thereafter, the patient made a rapid recovery, and he was discharged from the hospital a few days later. The fate of the two shadows seen in the bile duct on roentgenologic examination and purported to be calculi is open to speculation. If due to stones, it is possible that they fell out of the duct when the tube was removed. Since ether was not used in this case for the expulsion of the stones, it could not be the cause for their disappearance. At the time of writing, five years since the operation, the patient is well and free from symptoms.

Case 2.—B. M., a white woman, aged 46, entered the Mount Royal Hospital with the complaint of pain in the right upper quadrant of the abdomen. The onset of the present illness dated back two weeks previously, when she was seized with an attack of pain, colicky in character and confined to the right upper abdomen. The pain was accompanied by nausea, vomiting, and jaundice. The patient had had similar attacks of pain at intervals of three to four months for the past six years. She had always been in good health except for an appendectomy done 20 years previously.

Physical Examination.—The physical findings on admission to the hospital were briefly as follows: The patient was well developed and somewhat obese and did not appear acutely ill; the skin was icteric. The heart and lungs were normal; blood pressure was 140/80. The abdomen was slightly pendulous, soft, and free from tenderness or spasticity.

Laboratory Findings.—The urine was essentially negative except for the presence of bile. The red blood cells numbered 4,100,000; the white blood cells, 7,600, and hemoglobin was 85%. The blood chemistry findings were indicative of biliary obstruction.

Operation was performed two days after hospitalization. A right rectus incision was made to explore the gall bladder and common bile duct. The former contained several stones, of various sizes. The common duct was dilated and was therefore opened for exploration. Several small calculi and agglutinated debris were removed from the duct. The patency of the duct was then tested by passing through it a soft rubber catheter and irrigating it with isotonic sodium chloride solution. When the duct proved to be free from obstruction, a short-armed T-tube was placed within its lumen and fixed in position with sutures placed in the duct on either side of the tube. The abdominal wound was then closed in layers.

The patient recovered from the operation but the jaundice persisted, although to a less marked degree. The T-tube was therefore left undisturbed, and the patient was sent home with the tube still draining bile.

On the 23d postoperative day the patient suddenly felt faint and experienced a sharp pain in the abdomen; thereupon, she released the clamp from the T-tube. This was followed immediately by a gush of bright red blood from the indwelling catheter. The patient became very weak and was taken back to the hospital in a state of semishock.

On admission to the hospital the patient showed all the features of profuse hemorrhage. The pulse was rapid, weak, and thready and respirations were labored. The abdomen was tense and tender, and there was a continuous stream of blood flowing through the T-tube. She was given an immediate blood transfusion, and the indwelling T-tube was removed. She rallied somewhat, but not sufficiently to indicate that all bleeding has ceased. Accordingly, the patient was given another blood transfusion and taken to the operating room for an exploratory laparotomy.

On opening the abdominal cavity, there were found several hundred cubic centimeters of blood in the peritoneal cavity. The common duct was opened and explored; however, no active bleeding point could be found anywhere along its mucosal surface. There was found, however, a superficial erosion in the mucosa of the duct, which could have been the cause of the bleeding. However, since all bleeding had stopped at this time, it was left undisturbed. A good-sized vein was found coursing along the anterior surface of the duct, and it was ligated as a precautionary measure. Thereafter, the patient made an uneventful recovery and has not bled again.

EVALUATION

A striking feature of the incidence of choledochal bleeding secondary to an indwelling T-tube is the rarity with which it occurs. The severity of the condition is variable and depends to a large degree on the caliber of the bleeding vessel and the rate and amount of the blood loss. A few patients have little bleeding with mild symptoms, but others have profuse hemorrhages and rapidly develop shock, which makes them poor surgical risks and which must be relieved at once, sometimes through surgical intervention. The interval between the time of first operation and the onset of bleeding is also variable and depends on the rapidity with which a blood vessel becomes eroded and starts to bleed. In the present series it occurred on the 10th day in one patient and on the 23d day in the other.

Physical examination of a patient with choledochal bleeding is unlikely to provide any direct evidence as to the exact cause of the bleeding, although it is reasonable to assume that it is the result of trauma to the mucosal lining of the duct induced by the mechanical irritation of the indwelling T-tube. The general condition of the patient varies with the amount and rapidity of the blood loss. A patient having lost a small amount of blood may have mild symptoms and is in good health; at the other extreme is a patient who presents the clinical features of profound hemorrhage and a picture of shock. In the intermediate group are patients in whom the symptomatic effects of the bleeding are not severe but who often have latent manifestations of hemorrhage which can be detected only by careful search or by special clinical investigations; the assessment of a patient may be misleading if this is not remembered. The gravity of the condition, as judged both subjectively and objectively, is directly related to the severity and duration of the bleeding. Both our patients presented clinical signs and symptoms of considerable loss of blood. It was also apparent that the bleeding originated in each case in the wall of the duct. It has not been possible, however, to correlate these features with the size of the bleeding vessel, although it must be assumed that the involved vessel was of a good size to account for the profuse hemorrhage.

In considering the etiology of this condition, attention will be confined to the factors leading directly to its development. Since ether was not introduced into the duct in any of our cases, it cannot be regarded as an etiological factor in the causation of the bleeding. In all likelihood, the fundamental disturbance was an erosion into a blood vessel within the wall of the duct brought about by the indwelling T-tube. If this is true, it must be expected that the tendency to bleed

would be reduced or be completely stopped when the tube is removed, if for no other reason than that. The observation which supports this view is that relief of bleeding frequently follows the withdrawal of the tube, although this is not always the case. Of the reported cases, one was treated conservatively and the other by operation. In the first instance, the mere removal of the T-tube was sufficient to effect prompt cessation of the bleeding. In the second case, however, an emergency laparotomy had to be done when it became evident that bleeding could not be controlled by conservative means, such as removal of the tube.

As already indicated, the most plausible explanation for the development of bleeding in each of our patients is that it was due to mechanical irritation of the duct induced by the indwelling T-tube. It must be recognized, however, that conditions aside from trauma to the duct could have initiated the bleeding. There still remains a group of cases in which no correlation exists between the presence of the tube in the duct and the development of hemorrhage; hence other etiologic factors must be sought to explain this pathologic process.

It is not within the scope of this paper to enumerate all the various factors concerned in the production of ductal bleeding, but some of these may be mentioned to advantage. Thus, angiomatous formation in the duct, or aneurysmal dilatation and thinning out of the ductal artery, although rare occurrences in this location, may nevertheless occur and give rise to profuse hemorrhage. Also, various inflammatory conditions involving the common bile duct may conceivably give rise to varying degrees of ductal bleeding. Lastly, there are cases in which vitamin K deficiencies may contribute to the bleeding and should therefore be corrected.

In all instances of ductal bleeding loss of blood must be combated as far as possible by blood transfusions and should be given in sufficient quantity to counteract the rapidly developing anemia. Vitamin K should be administered in large doses, preferably by the parenteral route. The T-tube should be removed at once so as to prevent further irritation and bleeding. In some instances, the mere withdrawal of the tube is sufficient to control bleeding; such was the case in our first patient. In other instances, the situation cannot be corrected by conservative measures alone; under these circumstances more time is lost than gained by prolonging all palliative measures. In a patient in whom the state of anemia is well controlled by a well-planned preoperative treatment which reduces the operative hazard, thorough investigation of the source of bleeding should be undertaken. The surgeon may make a laparotomy, explore the duct, and correct any abnormality which may be found. It must be remembered, however, that the site of origin of the bleeding is not always obvious when a laparotomy is performed. Under these conditions, and especially in the case of a very ill patient in whom extensive investigation is prohibitive, it is judicious to be content with tying off the vessel to the duct. This was done in one patient, with effective results.

SUMMARY

Two cases of massive bleeding from the common bile duct consequent to irritation from an indwelling T-tube are presented. The methods used in control of such bleeding are generally discussed.

RELATION OF PORTAL VENOUS PRESSURE TO OCCLUDED HEPATIC VENOUS PRESSURE

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THE OPERATIONS of portacaval anastomosis and hepatic artery ligation are predicated upon the fact that these procedures, by diverting blood from the liver, lower the pressure in the portal system and in the varices which have formed in that system. While it is easy to demonstrate at operation that there is an immediate fall in pressure in the portal vein following either procedure, there has been some question concerning the length of time that the pressure remains lowered, since it has been demonstrated repeatedly in the experimental animal that these efforts at diversion of blood are compensated by an increase in flow through collateral systems.

Some assistance in the solution of this problem was obtained when, in 1951, Meyers and Taylor [1] demonstrated that by occlusion catheterization of an hepatic venule one could obtain a reasonably accurate estimation of the portal venous pressure. They showed that in 12 normal patients the mean occlusion catheter pressure was 4.8 mm. Hg, while in 7 patients with cirrhosis the mean pressure was 20 mm. Hg, varying from 11.5 to 32 mm. Hg. These observations were confirmed and extended by Paton, Reynolds, and Sherlock,[2] who demonstrated that equally accurate readings could be obtained from any branch of the hepatic system. They also pointed out that the only clinical entity besides cirrhosis of the liver in which the occluded hepatic venous pressure was likely to be elevated was in heart failure. These observations have been substantiated by Krook,[3] Balfour, Reynolds, and others,[4] and ourselves.

The technique of the method is not difficult. A Cournand end-recording catheter is passed into the venous system through an antecubital vein, preferably the medial branch. The catheter is directed through the right auricle, into the inferior vena cava, and, by manipulation under the fluoroscope, into an hepatic vein as far as it can be pushed. The catheter must occlude or be wedged into the vein, since if it is not a much lower free venous reading will be obtained.

The accuracy of the occluded hepatic venous pressure as a measure of the portal venous pressure was tested further at operation. After the catheter had been placed in the hepatic vein, the portal pressure was measured at open operation. In Table 1 the results in five patients with long-standing cirrhosis of the liver are shown. It is obvious from these measurements that in the cirrhotic liver the high portal pressure is reflected accurately in the occluded hepatic venous pressure.

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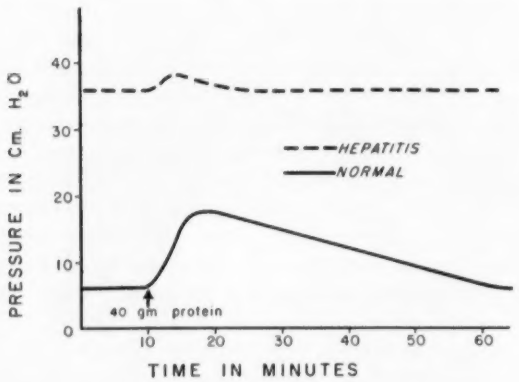
In order to determine whether an increase of splanchnic flow is reflected in the occluded hepatic venous pressure, a small group of patients with cirrhotic livers were compared with the normal patient after ingestion of a large amount of protein. The Figure shows a sample of the results obtained. After a normal control period, 40 gm. of protein extract was fed by stomach tube. In the normal patient there was an immediate and sustained rise of occluded hepatic venous pressure. In the cirrhotic patient, however, a slight rise occurred with a rapid return to the control level. Kelly * has performed a similar experiment and made measurements in terms of

TABLE 1.—*Hepatic-Wedge and Portal Venous Pressure Measurements Obtained at Operation*

Patient	Portal Venous Pressure, Mm. Hg	Occluded Hepatic Venous Pressure, Mm. Hg
V. R.	35-37	33-34
H. M.	34-36	37
F. L.	28-30	21-24
J. S.	30-33	30-33
L. G.	24-31	20-21



flow and oxygen consumption, rather than pressure. He found that there was about a 55% rise in both measurements in the normal, whereas in the cirrhotic patient there was no increase above 25%. The actual figures on the controls were an average of 1,090 cc. per minute, per square meter in the normal group, as opposed to 865 cc. a minute per square meter in the cirrhotic subjects.

Occluded hepatic venous pressure measurements were obtained on two patients who had hepatic artery ligations (in both patients the artery was ligated in the hilus of the liver before the division into right and left branches), on two patients who had end-to-side portacaval anastomoses, and on one patient who had a splenorenal anastomosis. All these patients were operated upon because of bleeding from esophageal varices secondary to cirrhosis of the liver. These results are summarized in Table 2.

* Kelly, J. J.: Personal communication to the authors, from the State University of New York College of Medicine at New York City, in Brooklyn.

REPORT OF CASES

CASE 1 (UC 30675).—I. G., a 37-year-old white woman, bled on five separate occasions from esophageal varices secondary to cirrhosis of the liver. In 1951 the hepatic artery was ligated. The pressure in the portal vein fell from 330 mm. of saline, before operation, to 125 mm. of saline, immediately after operation. After a stormy course the patient recovered. She now has ascites but has had no further hemorrhages. Hepatic-occluded pressure measured on Jan. 15, 1954, showed readings of 402, 397, 353 mm. of saline, with a free pressure of 175 mm.

CASE 2 (SFH 20481).—D. S., a 35-year-old white woman, bled severely in March, 1952. A diagnosis of esophageal varices secondary to cirrhosis of the liver was established at that time. A second small hematemesis occurred. On March 26, 1953, the hepatic artery was ligated. Pressures in the portal vein fell from 310 to 170 mm. of saline after the ligation. She had no further hemorrhages but has been ill with recurrent bouts of right upper quadrant pain and fever associated with positive blood cultures of a Salmonella organism. Hepatic-occluded pressure measurements on Jan. 19, 1954, were 290 and 320 mm. of saline. On protein feedings the pressure rose to 460 mm. after 15 minutes.

CASE 3 (VA 6576).—A. R., a 56-year-old Filipino man was found to have large esophageal varices secondary to cirrhosis of the liver in June, 1949, after he had had a severe gastrointestinal hemorrhage. In August, 1949, a side-to-side portacaval anastomosis was constructed. The portal pressure fell from 350 to 260 mm. of saline. Since operation the patient has had no

TABLE 2.—*Postoperative Measurement of Occluded Hepatic Venous Pressures in Cirrhotic Patients*

Case	Operation	Date	Portal Pressure, Mm. Saline: Pre-operative	Portal Pressure, Mm. Saline: Post-operative	Occluded Hepatic Venous Pressure, Mm. Saline	Time Elapsed from Operation to Pressure Record
1.....	H. A. L.	1951	330	125	402	3 yr.
2.....	H. A. L.	1953	310	170	320	6 mo.
3.....	P. C. A.	1949	350	260	330	4½ yr.
4.....	S. R. A.	1953	220	170	220	6 mo.
5.....	P. C. A.	1953	420	206	300	4 mo.

further hemorrhages, but has been plagued with repeated skin infections. Laboratory tests of liver function have shown progressive deterioration. On Jan. 14, 1954, hepatic-occluded pressure measurements ranged from 330 to 360 mm.

CASE 4 (SU 622).—F. L., a 52-year-old Chinese man, was found to have cirrhosis of the liver and esophageal varices after a severe intestinal hemorrhage. A large spleen was noted. In March, 1953, the hepatic-occluded pressure was noted to be 374 mm. One week later, a splenectomy and splenorenal anastomosis were performed. The portal pressure fell from 330 to 380 to 170 mm. of saline. The patient has had no further hemorrhages. On Dec. 12, 1953, the occluded pressure was found to be 220 mm.

CASE 5 (SFH 22631).—V. R., a 49-year-old white woman with a known diagnosis of cirrhosis, entered with ascites and gastric hemorrhages of moderate severity. In March, 1953, a side-to-side portacaval anastomosis was constructed. The pressure fell from 420 to 206 mm. of saline. The patient had a very stormy course, became jaundiced, and lost large quantities of fluid through the abdominal wound. Four months later the occluded pressure measured 300 mm. of saline. The patient died two weeks after this measurement.

COMMENT

The blood supply to the liver is unique in its organization. The teleological reason for this double circulation, according to Himsworth, is that the hepatic artery acts as a safety supply of blood under higher pressure and oxygen tension in the event of impairment of the venous supply in such situations as shock. While

some species are able to use more oxygen from venous blood, others are not, and protect themselves by increasing the blood supply reciprocally through the hepatic artery. This reaction can be demonstrated in the dog liver through colored injection preparations through the portal vein and hepatic artery.[5] After construction of an Eck fistula, there is evidence of an increased supply through a dilated hepatic arterial system. When a graft is placed between the aorta and the proximal stump of the portal vein in the dog with an Eck fistula, the dilated hepatic arterial system constricts down as the portal system dilates up.

Further evidence of the presence of a compensatory arterial supply in the dog is noted in the difficulty investigators have found in producing ischemia in the liver. It is necessary to ligate not only the hepatic artery but all the various attachments of the liver. Small arteries entering the liver directly from the aorta have been noted. It seems reasonable to suppose that such collaterals exist in the human.

If one accepts the clinical evidence that the hepatic-occluded pressure is approximately equal and parallel to the portal venous pressure, as well as the experimental evidence, it would appear that it is extremely difficult to lower the portal pressure for any length of time because of the efforts of the body to compensate for its loss of critical supply. If this compensation does not take place, the liver responds by a disorganization of its functions and failure of regeneration. Since this is a general physiological response when blood is diverted from an organ below a critical level. it would be most surprising if the liver responded otherwise.

The various reports on the benefits of portacaval anastomosis and hepatic artery ligation have suggested that this benefit was obtained by lowering the portal pressure. There is no doubt that the pressure does fall at the time of surgery, but there is considerable doubt that the pressure remains lowered for any length of time. In the five cases in which we have studied, it has not. In one of the two cases Krook studied, the pressure, which had been 290 mm. before operation, was 240 mm. four weeks after operation. Reynolds and his colleagues studied five patients treated by hepatic arterial ligation four to eighteen months postoperatively. They found the average measurement only 11% lower than the preoperative measurement and concluded that the operation failed to lower effectively the portal pressure.

As none of our cases has been examined at necropsy, it is conceivable that the rise in portal pressure following the initial fall may be due to closure of the anastomosis. This objection will not hold for the eventual rise in pressure following ligation of the hepatic artery, however.

It is also known that the pressure in the portal system varies. Dye and his co-workers[6] have noted this variation under medical management, a point, incidentally, which throws some doubt on the value of the disappearance of varices as a measure of an effective decompression. We have two patients being followed at the present time in whom the occluded pressure measurements have fallen when taken at three-month intervals. Both have ascites, and neither has demonstrable varices.

If it is true then, as some clinical reports would suggest, that patients who have had a portacaval anastomosis for cirrhosis of the liver are improved, this improvement must be due to some reason other than a permanent lowering of the portal hypertension.

SUMMARY

The occluded hepatic venous pressure is approximately equal to the portal pressure and changes parallel to the portal pressure.

The occluded hepatic venous pressure is characteristically elevated in cirrhosis of the liver.

Changes in the splanchnic flow are much less marked in the patient with cirrhosis of the liver than in the normal patient.

Evidence is presented that the fall in pressure obtained after ligation of the hepatic artery or portacaval anastomosis is not sustained.

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STUDIES ON REDUCTION OF INTESTINAL FLORA

Preoperative Treatment of Patients with Lesions of Colon or Rectum

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MARSHALL, Bratton, White, and Litchfield,[1] in 1940, published a report of investigations made with sulfaguanidine, a sulfonamide showing relatively little tendency to being absorbed. Its use had enabled them to reduce the number of colibacilli in the fecal flora of mice, and they recommended it for the treatment of infectious intestinal diseases in humans.

After this, sulfaguanidine was used preoperatively to reduce the coliflora prior to surgical intervention involving the colon or rectum. There was some dissatisfaction with this remedy, however, as some of it was absorbed and its effect on the coliflora was rather uncertain.*

The synthesization and testing of succinylsulfathiazole and phthalylsulfathiazole by Moore and Miller [4] and Poth and Ross,[5] respectively, was therefore a considerable advance in this field. Treatment with these drugs reduced the coliflora in the feces to less than 1,000 bacteria per gram in 93% of the patients in five to seven days. The enterococci, on the other hand, either were unaffected or increased in number simultaneously with the reduction of the colibacilli. The effect on the spore-forming anaerobic rods was likewise only slight.

The appearance of streptomycin as the first antibiotic effective against both Gram-negative and Gram-positive bacteria was greeted optimistically, as it was considered to constitute a better means of reducing the intestinal flora than the sulfonamides. It was particularly advantageous that orally administered streptomycin was not absorbed, but was discharged with the feces.

Reimann, Price, and Elias [6] and Zintel, Wiley, Nichols, and Rhoads [7] found that streptomycin was effective, but Rowe, Spaulding, Madajewski, and Bacon [8] and Lockwood, Young, Bouchelle, Bryant, and Stojowski [9] advised against its use, as they had found that its effects were not better than those of phthalysulfathiazole, and in many cases a resistant coli strain developed. They, therefore, recommended that streptomycin be restricted to postoperative complications and that it be used sparingly for preoperative treatment.

After the discovery of chlortetracycline (Aureomycin), Dearing and Heilman [10] investigated its effects on intestinal flora in 66 patients. The colibacilli were eliminated completely in 90% of the cases by ingestion of 3 gm. daily for one and one-half to six and one-half days. Simultaneously, however, Pseudomonas aeruginosa and Proteus bacteria appeared in the stools of 60% of the patients. Spore-

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* References 2 and 3.

forming anaerobic bacteria were completely eliminated, and in just above one-third of the cases the entire intestinal flora was eliminated (with the exception of yeast cells).

Oxytetracycline (Terramycin) was first produced in 1950, and its therapeutic and antibiotic effects closely resembled those of chlortetracycline. Up to 1952, the Mayo Clinic had treated 2,000 patients with these antibiotics prior to surgical intervention.[11]

Chloramphenicol (chloromycetin) is effective against Proteus bacteria, as is streptomycin. Chlortetracycline and oxytetracycline do not affect these bacteria. Chloramphenicol is hydrolyzed and rendered inactive by an enzyme formed by coli and Proteus bacteria and Bacillus subtilis.[12] In confirmation of this, Dearing and Heilman [13] found the drug to have only uncertain effects on the fecal flora.

The first to point out the importance of determining bacterial resistance when attempting to reduce the intestinal flora were Andina and Allemann.[14] They commenced by giving their patients chlortetracycline or oxytetracycline and determined the resistance of the bacterial flora so that they thereafter could choose the antibiotic or the combination of antibiotics most effective in the individual case.

PRESENT INVESTIGATION

Technique.—The feces specimens were transferred from the bedpan to sterile cardboard boxes with as little delay as possible and were then placed in a refrigerator until the bacteriologic examination could take place.

A sample of the intestinal lavage was likewise placed in the refrigerator (intestinal lavage here refers to 0.75 liter of water infused into the bowel three times).

Cultures from the mucous membrane of the bowel were taken during the operation with a cotton swab, which was well rubbed on the membrane just inside the site of resection. The swab was then placed in 2 ml. of broth. One to 2 hours later the suspension was spread on agar and, together with the refrigerated samples, investigated bacteriologically within 24 hours. Thus, the samples were kept at a temperature of 0 C. for 24 hours at the maximum, usually being so stored for only a few hours.

A sterile bottle containing some glass beads was weighed, and an almond-sized lump of feces was transferred to the bottle and weighed. The feces was then dissolved in 10 ml. of saline by thorough shaking. From this suspension a series of dilutions were made, graduated from 10^{-1} to 10^{-6}. Fluid feces was diluted directly from 0 to 10^{-5}.

By means of a platinum loop holding approximately 7 mg., the dilutions were then spread on four sets of plates. Each plate was divided into four sections, corresponding to four different dilutions. The plates consisted of the following media:

1. Bromthymol-lactose agar, for counting the lactose-fermenting and non-lactose-fermenting Gram-negative rods
2. Blood agar with 0.03% sodium azide, for counting Gram-positive cocci
3. Blood agar, serving chiefly as controls for the two preceding plates
4. Blood agar for the incubation of the anaerobic spore-forming rods. Before inoculation of the plates, the fecal dilutions were heated to 80 C. for 15 minutes in order to kill the non-spore-forming bacteria:

After incubation at 37 C. for 24 hours, the colonies were counted. The number of different bacteria could then be calculated per gram of feces, each bacterium being presumed to have given rise to a colony.

The resistance of each strain was then determined with regard to streptomycin, penicillin, sulfathiazole, chlortetracycline, chloramphenicol, and oxytetracycline. Later, penicillin and chlortetracycline were replaced by bacitracin and neomycin.

Patients.—The patients came from Department I of Copenhagen's Kommunehospital (KH) and from Department D of Bispebjerg Hospital (BBH). The 40 patients from KH had lesions

of the colon or rectum, the majority being cancer. Seventeen of these patients were treated with phthalylsulfathiazole (12 gm. the first day, followed by 6 gm. daily for at least five days).

The remaining 23 patients were treated according to the outcome of the resistance determinations. Eight were given 3 gm. oxytetracycline daily for three to five days. Thirteen were given oxytetracycline (3 gm.) for four to five days, as well as 2 gm. of streptomycin daily (administered orally) for the last two days.

Two patients were given oxytetracycline daily for three days, followed by chloramphenicol (3 gm.) daily for two and four days, respectively.

The 26 patients from BBH were suffering from operable diseases of the bladder. (These patients are included in Jensen's investigations [15] on the dependence of flora in the urinary tract on the fecal flora.) Twenty-three were given 3 gm. of oxytetracycline daily for four days, and 1.5 gm. of streptomycin was given orally for the last two days of the treatment. Three patients received 3 gm. of oxytetracycline daily for 1½, 3, and 4 days, respectively, followed by 3 gm. of chloramphenicol for 2½, 1¼, and 11 days, respectively. Two of the latter were, furthermore, given 1.5 gm. of streptomycin daily for two and five days, respectively.

TABLE 1.—*Schematic Survey of the Effect of Various Antibiotics on the Intestinal Flora**

		Bacteria Present Before Treatment		Bacteria Present During Treatment		Growth from Intestinal Swab During Operation	
Bacteria	Treatment	No.	%	No.	%	No.	%
Lact. + rods	Phthalylsulf.	17:17	100	17:17	100	10:15	67
	Terramycin	8: 8	100	8: 8	100	2: 7	29
	Terra. + strep.	12:13	92	12:13	92	0:13	0
Cocci	Phthalylsulf.	17:17	100	17:17	100	15:15	100
	Terramycin	7: 8	88	8: 8	100	1: 7	14
	Terra. + strep.	13:13	100	13:13	100	10:13	77
Sporulating anaerobes	Phthalylsulf.	17:17	100	17:17	100	6:13	40
	Terramycin	4: 8	50	4: 8	50	0: 7	0
	Terra. + strep.	8:13	62	10:13	77	0:13	0
Lact. — rods	Phthalylsulf.	3:17	18	4:17	24	3:15	20
	Terramycin	2: 8	25	6: 8	75	2: 7	29
	Terra. + strep.	1:13	8	6:13	46	2:13	15
Proteus	Phthalylsulf.	0:17	0	0:17	0	0:15	0
	Terramycin	0: 8	0	2: 8	25	2: 7	29
	Terra. + strep.	3:13	23	7:13	54	3:13	23
Total	Phthalylsulf.	17:17	100	17:17	100	15:15	100
	Terramycin	8: 8	100	8: 8	100	5: 7	71
	Terra. + strep.	13:13	100	13:13	100	11:13	85

* Treated with Sulfathalidine (phthalylsulfathiazole), 17 patients; treated with Terramycin (oxytetracycline), 8 patients, and treated with Terramycin + streptomycin, 13 patients.

Prior to treatment, all the patients were given a laxative, and during the treatment the feces were kept semifluid, with the help of magnesium sulfate. They were also kept on a low-residue diet, approaching a broth diet.

EXPERIMENTAL RESULTS

From Table 1, it can be seen that the reduction of coli bacteria was far more certain when the preoperative treatment consisted of oxytetracycline and streptomycin than when the patients received phthalylsulfathiazole. Growth of bacteria was found in cultures obtained from the intestinal lumen of 10 of the 15 patients treated with phthalylsulfathiazole, whereas no growth was observed in any of the 13 cases in which both oxytetracycline and streptomycin were administered. This can also be seen from Figure 1.

There was no reduction in cocci subsequent to treatment with phthalylsulfathiazole, whereas oxytetracycline plus streptomycin gave varying results (Fig. 3). From

Table 1 it appears that fewer cocci were found when oxytetracycline was given alone than when it was combined with streptomycin. This is due to streptomycin having been given in cases in which the resistance determinations showed the existence of oxytetracycline-resistant bacteria. A number of these bacteria were cocci, and this fact of course affects the results shown by the oxytetracycline plus streptomycin group, especially as these cocci also became resistant to streptomycin quickly.

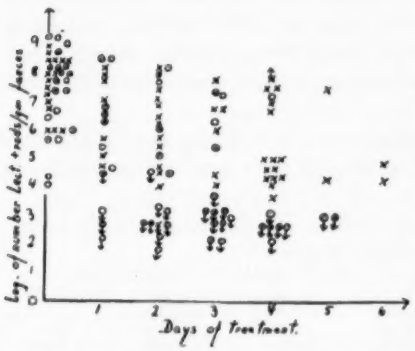

Fig. 1.—Graphic presentation of the effects of new antibiotics on the lactose-fermenting-rod bacilli of the intestine.

Crosses indicate patients treated with phthalylsulfathiazole (17); circles, patients treated with oxytetracycline (8); circles with dot, patients treated with oxytetracycline plus streptomycin (13); upward-directed arrows, a number of bacteria greater than the number plated, and downward-directed arrows, a number of bacteria less than the number plated.

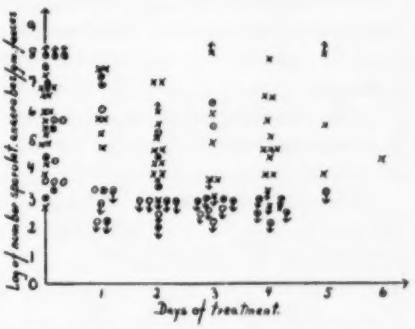

Fig. 2.—Graphic presentation of the effects of new antibiotics on intestinal sporulating anaerobes.

Crosses indicate patients treated with phthalylsulfathiazole (17); circles, patients treated with oxytetracycline (8); circles with dot, patients treated with oxytetracycline plus streptomycin (13); arrows directed upward, a number of bacteria greater than the number plated; arrows directed down, a number of bacteria less than the number plated.

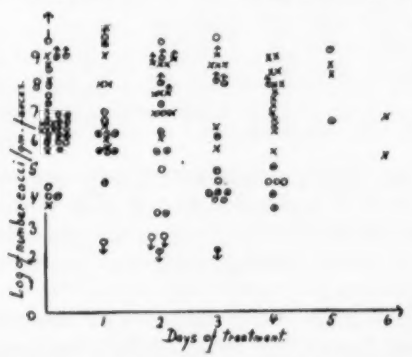

Fig. 3.—Graphic presentation of the effect of new antibiotics on intestinal cocci.

Crosses indicate patients treated wth phthalylsulfathiazole (17); circles, patients treated with oxytetracycline (8); circles with dot, patients treated with oxytetracycline and streptomycin; arrows directed upward, a number of bacteria greater than the number plated; arrows directed downward, a number of bacteria less than the number plated.

Oxytetracycline plus streptomycin also showed better results than phthalylsulfathiazole in reduction of spore-forming anaerobic bacteria. This can be seen from Table 1 and Figure 2. Proteus and non-lactose-fermenting rods appeared in many cases treated with oxytetracycline, and they could not always be eliminated, even

after streptomycin was introduced. In only four cases out of 20 was it possible to reduce the intestinal flora to such an extent that no growth was apparent in the samples taken during the operation (apart from yeast cells).

If the results of the preoperative treatment with oxytetracycline and streptomycin obtained at KH and BBH are compared, it will be seen that they are similar, except for the considerable number of non-lactose-fermenting rods found in patients from BBH.

Chloramphenicol was administered in five cases in which bacteria resistant to both oxytetracycline and streptomycin were found. These bacteria were not successfully eliminated in any of these patients, in spite of their sensitivity to chloramphenicol.

Thus, oxytetracycline, supplemented with streptomycin during the last two days of treatment, was better fitted for reducing the coli flora and the spore-forming

TABLE 2.—*Schematic Survey of Effect of Oxytetracycline plus Streptomycin on Intestinal Flora in the Two Patient Materials**

Bacteria	Oxytetracycline + Streptomycin	Bacteria Present Before Treatment		Bacteria Present During Treatment		10,000 Bact./Ml. or More in Preop. Lavage		1,000 Bact./Ml. or More in Preop. Lavage		Bact. in Preop. Lavage	
		No.	%	No.	%	No.	%	No.	%	No.	%
Lact. + rods	KH, Dep. I	20:21	95	20:21	95	2:21	10	2:21	10	3:21	14
	BBH, Dep. D	23:23	100	23:23	100	0:23	0	0:23	0	0:23	0
Cocci	KH, Dep. I	20:21	95	21:21	100	7:21	35	18:21	86	18:21	86
	BBH, Dep. D	23:23	100	23:23	100	9:22	41	14:22	64	16:23	70
Sporulating anaerobes	KH, Dep. I	12:21	52	14:21	67	2:21	10	2:21	10	2:21	10
	BBH, Dep. D	10:10	100	10:10	100	1:10	10	1:10	10	1:10	10
Lact. — rods	KH, Dep. I	3:21	14	12:21	57	4:21	19	5:21	24	5:21	24
	BBH, Dep. D	3:23	13	17:23	74	10:22	45	13:22	59	15:23	65
Proteus	KH, Dep. I	3:21	14	9:21	43	.....	..	.....	..	4:21	19
	BBH, Dep. D	2:23	9	9:23	39	.....	..	.....	..	5:23	22
Total	KH, Dep. I	21:21	100	21:21	100	11:21	52	18:21	86	18:21	86
	BBH, Dep. D	23:23	100	23:23	100	18:22	82	21:22	96	23:23	100

* KH, Dept. I, 21 patients; BBH, Dept. D, 23 patients.

anaerobic rods than was phthalylsulfathiazole. On the other hand, proliferation of non-lactose-fermenting gram-negative rods and cocci often took place. It was therefore desirable to find an antibiotic that was more successful in reducing the intestinal flora, and it seems that bacitracin and neomycin form a promising combination for this purpose.

Bacitracin and neomycin have the advantage of not being absorbed by the intestinal canal to any great degree, like streptomycin. These two antibiotics have a spectrum covering all the bacteria usually found in the intestine, and they must, therefore, be considered especially well suited to preoperative use.

Poth [16] gave 6 gm. of neomycin combined with 9 gm. of phthalylsulfathiazole daily to 300 patients and found that the bacterial flora was eliminated after two or three days' treatment.

Dearing and Needham † found that the administration of neomycin alone was sufficient to eliminate the anaerobic bacteria in most cases, but spore-forming

† References 17 and 18.

anaerobic bacteria persisted. They therefore supplemented their treatment with oxytetracycline. In this way, it was possible to reduce the intestinal flora in most cases, except for yeast cells.

Bacitracin has been given orally to human subjects in treating amebic dysentery. Bond, Vander-Brook, Wiley, and Nook [19] gave bacitracin to dogs and found an obvious reduction in Gram-positive cocci and anaerobic spore-forming rods. A combination of bacitracin and neomycin has hitherto been administered only in treatment of infants with infantile diarrhea, by Kadison and Borovsky.[20] They found that this combination cured the complaint more quickly than other antibiotic.

I therefore decided to investigate the effects of this combination on intestinal flora using the same method as that previously described. It was, however, decided to excise two pieces of the intestinal mucosa (each about 1 sq. cm.), in addition to taking swabs. The samples of the intestinal mucosa were incubated aerobically and anaerobically.

The patients treated preoperatively with bacitracin plus neomycin ‡ were all from Department I of KH and were all suffering from lesions of the colon or rectum. Thirty-two patients were given 3 gm. of bacitracin and 3 gm. of neomycin orally for three to four days. Nine were given 2 gm. of bacitracin and 2 gm. of neomycin orally for three days. Six received 1 gm. of bacitracin and 1 gm. of neomycin orally for three days. The results may be seen in Table 3.

Group I consists of 32 patients who received the largest dose, while Group II is composed of the 9 and 6 patients who were given the lower (2 and 1 gm.) doses. It will be seen from Table 3 that the effect of bacitracin plus neomycin on lactose-fermenting and anaerobic spore-forming rods corresponds to that of the oxytetracycline-streptomycin treatment, while the reduction of cocci, non-lactose-fermenting rods, and Proteus is far more dependable. Thus, in 89% of the cases in Group I (25 of 28 patients) the intestinal flora was eliminated, with the exception of yeast cells and bacteroids,§ while treatment with oxytetracycline plus streptomycin eliminated the flora in only 20% (4 out of 20 patients). Anaerobic and aerobic cultures of the intestinal mucosa in broth showed growth of bacteria in only 19% (5 of 26 cases).

The results in Group II were less satisfactory than those in Group I. Examination of the case histories of those patients in Group I in whom intestinal bacteria persisted in spite of treatment shows that in four of the five cases the results could be explained as due to deficient intestinal passage. Of the six patients in Group II to whom 1 gm. of bacitracin plus 1 gm. of neomycin was administered daily, four showed bacterial persistence. In none of these was the intestinal passage so restricted as to offer a reason for the reduced effects of the treatment. On this basis, it appears that this dosage for three days is insufficient, the best results being obtained by trebling the dose.

In 26 of the patients receiving 3 gm. of bacitracin and 3 gm. of neomycin daily, the concentrations of the drugs in the blood and urine were determined. In no case were there any traces of the drugs in the blood, and in the urine only 0.6% or less

‡ Bacitracin and neomycin were placed at my disposal by H. Lundbeck & Co., Copenhagen.

§ Bacteroids are small Gram-positive obligate anaerobic non-spore-forming rods that are usually considered to have no pathogenic effects.

TABLE 3.—*Schematic Survey of Effect of Combination of Bacitracin and Neomycin on Intestinal Flora**

Bacteria	Treatment Bacitracin + Neomycin Group	Bacteria Present Before Treatment		Growth from Swab During Operation		Bacteria Present in Intestine Incubated 24 Hr.		Growth from Last Preoperative Specimen of Feces		Growth from Preoperative Intestinal Lavage	
		No.	%	No.	%	No.	%	No.	%	No.	%
Lact. + rods	I	32:32	100	2:28	7	4:26	15	3:32	9	3:27	11
	II	15:15	100	2:14	14	4:14	29	4:15	27	3:13	23
Cocci	I	32:32	100	0:28	0	0:26	0	1:32	3	1:27	4
	II	15:15	100	1:14	7	3:14	21	1:15	7	1:13	8
Sporulating anaerobes	I	28:32	88	1:28	4	0:26	0	3:32	9	2:27	7
	II	15:15	100	0:14	0	3:14	21	5:15	33	1:13	8
Lact. — rods	I	8:32	25	0:28	0	1:26	4	2:32	6	2:27	7
	II	6:15	40	1:14	7	3:14	21	3:15	20	1:13	8
Yeast cells	I	0:32	0	21:28	75	20:26	77	28:32	88	19:27	70
	II	0:15	0	7:14	50	9:14	64	10:15	67	6:13	46
Total growth, excluding yeast and bacteroids	I	32:32	100	3:28	11	5:26	19	6:32	19	5:27	19
	II	15:15	100	3:14	21	8:14	56	7:15	47	4:13	31
Total growth, excluding yeast cells	I	—	—	—	—	14:26	54	—	—	—	—
	II	—	—	—	—	11:14	79	—	—	—	—

* Group I: 32 patients treated with 3 gm. of neomycin and 3 gm. of bacitracin daily for three to four days; Group II: 15 patients treated with 1 to 2 gm. of neomycin and 1 gm. of bacitracin daily for three days.

TABLE 4.—*Preoperative Treatment and Complications of Extirpation of the Rectum and Sigmoid with Opening of Intestine (Including Artifacts)**

Preoperative Treatment	No.	Temp. More Than 101.3 F First Postop. Week	Wound Infection	Peritonitis, Diffuse	Peritonitis, Local	Death	Cause of Death
No treatment	6 (48)	2	2	1	0	4	Peritonitis 1 Pulmonary embolism 2 Unknown 1
Phthalylsulfathiazole	22 (127)	3	7	2 (3)	0	3	Peritonitis 1 Carcinomatosis 1 Uremia (peritonitis) 1
Oxytetracycline + streptomycin	6 (23)	1	3	0	0	1	Pneumonia 1
Bacitracin + neomycin	5 (18)	0	0	0	0	2	Paralytic ileus and uremia 1 Pulmonary atelectasis and hemoperitoneum 1

* The figures in parenthesis in the column headed "No." indicate the total number of extirpations of the rectum and sigmoid flexure done in one stage.

TABLE 5.—*Preoperative Treatment and Complications of Resection of the Colon and Hemicolectomy*

Preoperative Treatment	No.	Temp. More Than 101.3 F First Postop. Week	Wound Infection	Peritonitis, Diffuse	Peritonitis, Local	Death	Cause of Death
No treatment	26	9	3	3	0	3	Peritonitis 1 Unknown; cardiac failure (?) 2
Phthalylsulfathiazole	62	15	5	2	3	5	Peritonitis 1 Pulmonary embolism 2 Uremia 1 Pneumonia 1
Oxytetracycline + streptomycin	11	7	1	0	0	2	Compression of superior mesenteric vein 1 Perforation of intestine supervening operation 1
Bacitracin + neomycin	10	0	1	0	0	0	

TABLE 6.—*Preoperative Treatment and Complications Following Resection of Rectum*

Preoperative Treatment	No.	Temp. More Than 101.3 F First Postop. Week	Wound Infection	Peritonitis, Diffuse	Peritonitis, Local	Death	Cause of Death
No treatment	10	2	1	0	0	2	Pneumonia 1 Unknown 1
Phthalylsulfathiazole	28	5	5	3	0	2	Peritonitis 2
Oxytetracycline + streptomycin	3	0	0	0	0	0	
Bacitracin + neomycin	6	1	1	0	0	0	

TABLE 7.—*Survey of Entire Material (Tables 4, 5, and 6)*

Preoperative Treatment	No.	Temp. More Than 101.3 F First Postop. Week	Wound Infection	Peritonitis, Diffuse	Peritonitis, Local	Death	Cause of Death
No treatment	42	13	6	4	0	9	Peritonitis 2 Pulmonary embolism 2 Pneumonia 1 Unknown 4
Phthalylsulfathiazole	112	23	17	7 (8)	3	10	Peritonitis 4 (5) Pulmonary embolism 2 Carcinomatosis 1 Pneumonia 1 Uremia 1
Oxytetracycline + streptomycin	20	8	4	0	0	3	Pneumonia 1 Compression of superior mesenteric vein 1 Perforation of intestine supervening operation 1
Bacitracin + neomycin	21	1	2	0	0	2	Paralytic ileus and uremia 1 Pulmonary atelectasis and hemoperitoneum 1

of the neomycin and 0.8% or less of the bacitracin administered were found. Correspondingly, no albumin or urinary casts were found in the urine consequent to the treatment.

Thus, in most cases in which there are no intestinal occlusions it is possible to reduce the intestinal flora to yeast cells and bacteroids by administering bacitracin and neomycin. Such satisfactory results have not been obtained with any of the other antibiotics.

Examinations of the feces 8 to 14 days after cessation of treatment showed that the normal intestinal flora was again present. This was true not only of those patients treated with bacitracin and neomycin, but also of those to whom oxytetracycline and streptomycin or phthalylsulfathiazole had been administered.

In order to show the importance of the reduction of intestinal flora from a clinical point of view, the case histories of patients at Department I of KH who had been operated on for diseases of the colon or rectum during the period from Jan. 1, 1946, to Jan. 3, 1953, were reviewed. It appeared that in 195 cases there had most likely been fecal contamination. From Tables 4, 5, 6, and 7, the number of postoperative infectious complications possibly due to such contamination can be seen. It will be noted that patients treated with bacitracin plus neomycin present fewer postoperative complications, and this is true of all the groups concerned. Likewise, no case of peritonitis was observed in any patient treated preoperatively with an antibiotic.

Thus, the clinical observations seem to support the use of bacitracin plus neomycin, even though it is not possible to prove their worth statistically, owing to the large number of other factors that could affect the postoperative course.

The only side-effects observed in connection with the treatment were a mycosis-like eczema in the region of the anus and genitals and stomatitis. These complications were found in a very few patients about a week after cessation of treatment.

COMMENT

Primary colon resection previously involved a high mortality rate. Fecal contamination must certainly have been mainly responsible for the insufficiency of the sutures at the site of resection and the peritoneal infectious processes. The Bloch-Mikulicz method reduced the possibility of these complications occurring, and peritonitis and abscess formation could for the most part be avoided. Another way of hindering contamination is based on the so-called closed technique, but neither of these methods was ideal, and the best solution to the problems involved undoubtedly lies in the elimination of the intestinal flora so that the operation can be performed under absolutely sterile conditions.

Phthalylsulfathiazole was effective mainly against the coli flora, and the experimental and clinical results were better than when no antibiotic was employed. However, a number of intestinal bacteria were not affected by the sulfonamides, and their effects on colibacilli were not dependable. Definite elimination was not obtained in most cases, as is seen from Table 1.

The administration of oxytetracycline plus streptomycin usually eliminated the coli bacteria as well as the spore-forming anaerobic rods, but resistant non-lactose-fermenting rods and Gram-positive cocci often proliferated. After some time a pure culture of Staphylococcus aureus appeared in the feces of patients at KH who had

been treated preoperatively with these two drugs in combination. This Staphylococcus was resistant to penicillin, sulfathiazole, chlortetracycline, oxytetracycline, and streptomycin, and often also to chloramphenicol (Eriksen [21]). At the same time, Finland and co-workers [22] and Dearing and Heilman [23] reported serious enteritis brought about by Staph. aureus in patients who had been treated with oxytetracycline.

Under such conditions, it is very important that an ideal intestinal antiseptic is available in the combination of bacitracin and neomycin. Preoperative administration of this combination eliminates all flora with the exception of yeast cells, and in some cases with the exception of bacteroids. This flora must be considered to be far less pathogenic than the usual millions of colibacteria, clostridia, and cocci of various types. This opinion is further supported by the clinical evidence available.

An additional advantage in the use of bacitracin and neomycin is that the drugs are not absorbed from the intestine but remain there in the postoperative period, when the intestinal passage is restricted.

If postoperative infections nevertheless arise, all the other universally effective antibiotics are still at one's disposal. Were these used preoperatively, it is unlikely that they would prove efficient in such cases, as most probably some resistant flora would appear. In this connection, it is necessary to add that the appearance of resistance to bacitracin and neomycin does not affect resistance toward other antibiotics.

Even though bacitracin- and neomycin-resistant strains have not been observed in the department concerned, it is of course impossible to assume that such strains cannot appear, just as they did in the case of oxytetracycline and streptomycin. It is therefore advisable when administering these drugs during routine preoperative treatment to control their effects by means of bacteriological examinations of the feces.

CONCLUSION

By administration of 3 gm. of bacitracin and 3 gm. of neomycin daily for three days, assuming that the intestinal passage is not too difficult and that the patient receives a low-residue diet, it is possible to reduce the normal intestinal flora content to yeast cells and bacteroids.

Clinically, the postoperative course is less complicated than for those patients not treated prior to surgical intervention on the colon or rectum.

The details of these investigations appear in three articles published in *Acta chirurgica scandinavica.*||

SUMMARY

After Poth had introduced succinylsulfathiazole and phthalylsulfathiazole in the preoperative treatment of patients with operable conditions of the colon or rectum, the risk involved in such operations was reduced.

On its appearance, streptomycin was also tried out but proved to be unsuitable, owing to the rapid development of resistance.

Dearing and Heilman investigated the effects of phthalylsulfathiazole, succinylsulfathiazole, chloramphenicol, and chlortetracycline and found that the last drug was best suited to the task of reducing the fecal flora.

|| References 24, 25, and 26.

Andina and Allemann used resistance determinations to guide them in their work on the reduction of fecal flora.

I treated 17 patients with phthalylsulfathiazole, while 49 others were given antibiotics on the basis of resistance determinations. Of the latter group, 8 were given only oxytetracycline; 36 received oxytetracycline and streptomycin, and 5 were given combinations of antibiotics which included chloramphenicol. It was found that oxytetracycline and streptomycin was the combination most frequently required for the reduction of intestinal flora. This combination was far more effective in reducing coli flora and the spore-forming anaerobic flora than was phthalylsulfathiazole. No particular effects of chloramphenicol were observed in the five cases in which this drug was used.

However, oxytetracycline and streptomycin-resistant bacteria often proliferated during this treatment, and as time passed, more and more cases were observed in which the feces developed into pure cultures of Staph. aureus. The search was therefore started for other antibiotics suitable for the reduction of the intestinal flora.

Bacitracin and neomycin in combination were given to 47 patients. A dose of 3 gm. daily of each drug for three days sterilized the intestine (with the exception of yeast cells and bacteroids) in nearly all cases in which there was no occlusion of the intestinal passage.

The absorption of these drugs was so negligible that there was no need to fear toxic side-effects.

In order to estimate the importance of the reduction of the intestinal flora from a clinical point of view, I reviewed 195 case histories in which it was probable that there had been fecal contamination during the operation. Of these, 42 had not been treated preoperatively; 112 had been given phthalylsulfathiazole; 20, oxytetracycline plus streptomycin, and 21 bacitracin plus neomycin. This investigation gave the impression of an easier postoperative course with fewer infectious complications in those who had been treated with bacitracin plus neomycin prior to surgical intervention. The clinical material was, however, too small and was not homogeneous enough to allow any definite conclusions to be drawn.

It is concluded that for the preoperative reduction of the intestinal flora, 3 gm. of bacitracin and 3 gm. of neomycin should be given daily for three days.

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MODES OF HEALING FOLLOWING SURGICAL CLOSURE OF EXPERIMENTAL ATRIAL SEPTAL DEFECTS

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BECAUSE the last few years have shown that surgical attack on interauricular septal defects in the human has now become a matter of practical concern, it is well to learn from the laboratory as much as possible about the patterns of healing which ensue when interatrial openings are closed surgically in experimental animals.

In previous publications we have described the experimental background and clinical application of a surgical technique, using an atrial "well," which affords access to all portions of the interatrial septum.* By means of this method, precise manipulations can be carried out within the interior of the heart so that atrial septal defects can be created and may then be closed despite considerable variation in size and location of the openings. This affords an opportunity to study different methods of closing such defects and to compare the different patterns of healing at appropriate intervals after repairs. A comparative analysis of the tissue response to these different methods was carried out by the killing of animals at intervals after operation and inspection of the repaired septums by the conventional methods of gross examination and also by microscopic study.

Previous publications on the use of tissue grafts in the cardiovascular system have been concerned chiefly with vessel replacement or vavular reconstruction. Fascial strips have been used to bridge interventricular septal defects [18]; the ultimate fate of the fascia has not been reported. Segments of fascia lata have been used to produce stenosis of the mitral valve in dogs [19]; massive thrombosis on the fascia usually resulted in death. Segments of vein or pericardium have been found to be unsatisfactory as valve leaflet replacements because of late contraction and fibrosis.† Free grafts of atrial appendage show early ischemic necrosis and late fibrous tissue replacement and contraction.‡

A tissue-graft placed within the heart should present certain desirable characteristics, including durability, ready availability, and a minimal excitation of surface

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† References 14, 17, and 19.

‡ References 2 and 16.

thrombus formation. It is material which can be trimmed easily to conform to the size and contour of the defect which is being treated. Published reports suggest that portions of atrial appendage, vein, or pericardium might be suitable when implanted to cover atrial septal defects. Changes of fibrosis and contracture did not appear to be disturbing or harmful, since the grafts were implanted on the atrial septum, where considerable contraction is permissible.

In a review of the use of plastic substances in surgery, Ingraham and his associates [11] noted minimal tissue reaction to methyl methacrylate (Lucite or Plexiglas), nylon, and polyethylene when they were used in many regions of the body other than the heart. In cardiovascular surgery, these substances have been used as tubes to bridge arterial defects,[4] to by-pass the pulmonic valve,[10] and as cardiac-valve prostheses.§ Frequently these prostheses have failed to function because of

Fig. 1.—Typical atrial septal defect created by working through a rubber well. Right atrial view with a probe placed in the coronary sinus.

thrombosis and obstruction. Martin and Essex [12] described early thrombus formation on the surface of small polyethylene discs introduced blindly to close experimental atrial septal defects. Although the thrombus was organized and endothelized within two to six months, the authors preferred to cover the plastic disc with a segment of everted vein. Hufnagel and Gillespie [9] devised ingenious, paired, plastic buttons which were joined to each other by a screw mechanism; they grasped the two sides of a septum, effectively occluding any orifice over which they were placed. They reported early endothelial growth over such buttons and ultimately a complete incorporation of the prosthesis into the septum. These various studies have already indicated the remarkable capacity of the heart to tolerate plastics when implanted onto the septum, but a number of questions were raised concerning the mechanism

§ References 1, 3, and 8.

of healing around these plastic materials. It would be important to know whether loose thrombus piles up from nonwettable plastic surfaces and thus presents a threat of embolization. It would be well to know whether cysts form around plastics when they are embedded in a living animal. It would be important to know whether plastics dislodge and migrate as a result of heart motion over long periods of time.

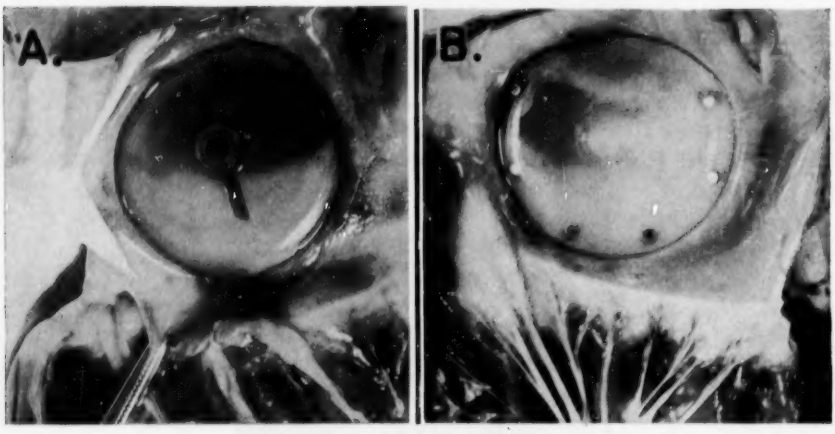

Fig. 2.—Plastic screw-on buttons of the type described by Hufnagel and Gillespie. An atrial septal defect has been occluded by this 3-cm. button fashioned from trifluorochloropolyethylene (Kel-F) plastic. The animal was killed immediately after operation. The defect is completely closed by the button. *A*, right atrial view; *B*, left atrial view.

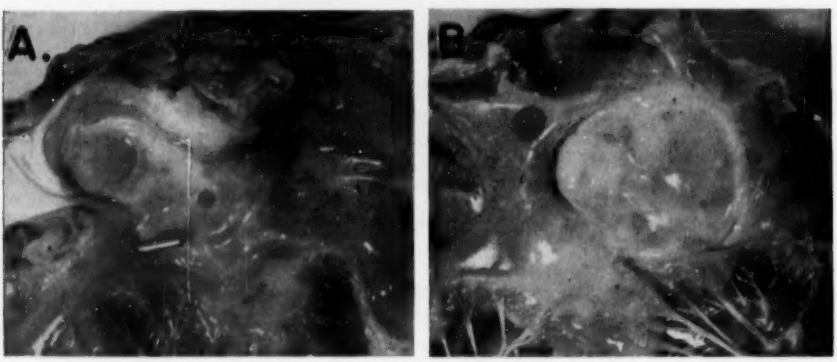

Fig. 3.—Plastic screw-on buttons (methyl methacrylate, 3 cm. in diameter) three months after operation. *A*, right atrial view. The button is almost indiscernible, since it is encased in a fibrous capsule lying immediately above and to the right of the probe in the coronary sinus. *B*, left atrial view.

Implantation of plastics in the heart should be critically examined with these questions in mind.

EXPERIMENTAL PROCEDURES

Studies were made after the following general types of surgical repair of atrial septal defect had been effected: (1) closure by plastic buttons which are joined to each other by a screw mechanism, and thus occlude a septal orifice (Hufnagel buttons); (2) suture coaptation of septal

defect edges; (3) suture fixation of various free tissue grafts to cover a septal opening. (4) suture fixation of various plastic sheets to occlude the septal orifice.

Adult mongrel dogs, ranging in weight from 17 to 26 kg., were used. With the animal under pentobarbital (Nembutal) anesthesia, the right pleural space was entered through the fifth interspace. A rubber "well" was attached to the lower part of the atrial wall and the right atrium then opened, as described in detail in previous communications.‖ Atrial septal

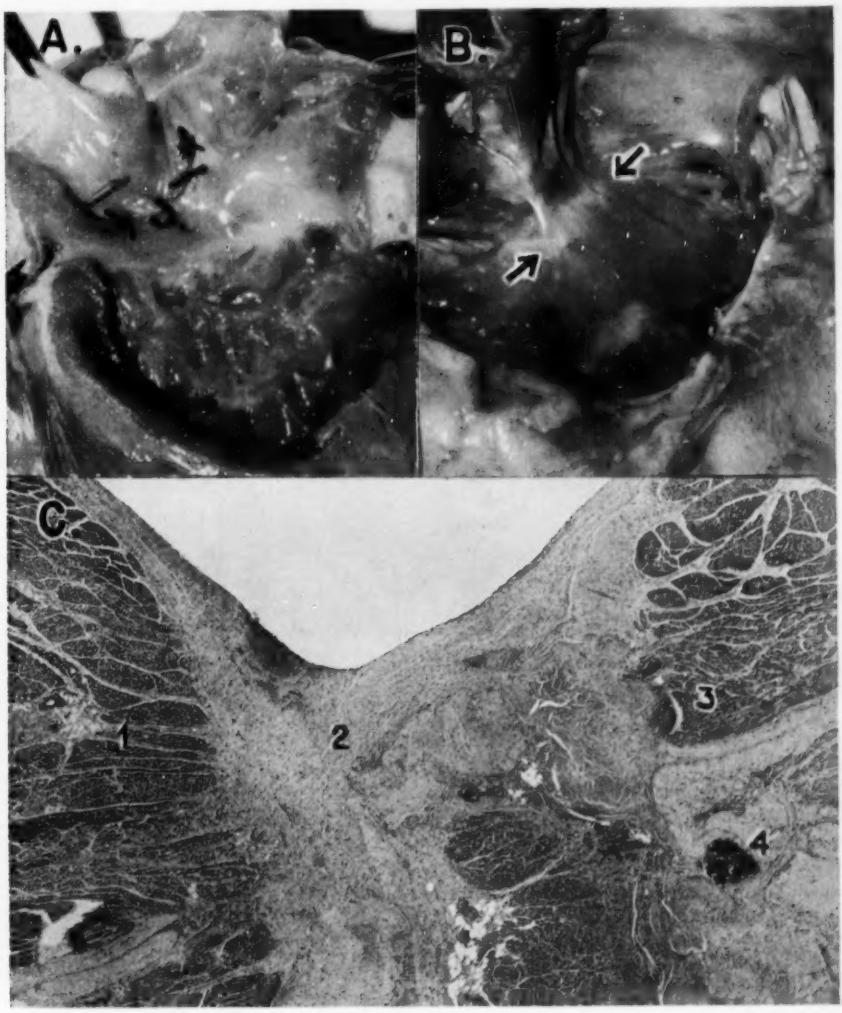

Fig. 4.—Closure of atrial septal defect by suture coaptation of its edges. *A*, animal killed immediately after closure of defect with four interrupted sutures of silk; right atrial view. A probe has been placed in the coronary sinus. *B*, specimen five weeks after operation; right atrial view. There is complete healing and endothelization of the closure area which lies between the two arrows. *C*, photomicrograph of an atrial septum eight weeks after suture closure of a defect. The opposed muscle edges of the septal defect are marked *1* and *3*. The fibrous scar resulting from union is marked 2. One silk suture may be seen (marked *4*). Hematoxylin and eosin stain; × 40.

‖ References 6, 7, and 18.

defects, ranging in diameter from 2.0 to 2.5 cm., were created by excision of tissue from the fossa ovalis. Each defect was then closed during the same operation by one of the methods hereafter described. The rubber "well" was removed and the auricle closed by interrupted nonabsorbable surgical (silk) sutures.

During operation, each animal received 250 to 500 ml. of citrated dog blood. During the time that the atrium was open into the "well," small amounts of 0.01% heparin solution were introduced every few minutes into the rubber appliance. Each animal received less than 0.5 mg. of heparin per kilogram of body weight.

After closure of the chest and aspiration of air from the pleural cavity, each animal was given an intramuscular injection of 300,000 units of penicillin G procaine and an intrapleural injection of 100,000 units of aqueous crystalline penicillin. A standard kennel ration of dog biscuit and raw, ground horse meat was offered daily. All animals were confined to cages and were not exercised after operation.

The following methods of defect closure were studied:

A. Closure of Defects with Plastic Screw-On Hufnagel Buttons.—With minor modifications of the design reported by Hufnagel and Gillespie,[9] two-piece screw-on buttons were machined from methyl methacrylate or trifluorochloropolyethylene (Kel-F). These buttons measured 2 or 3 cm. in diameter. The methyl methacrylate buttons were sterilized by soaking for at least 24 hours in 1 : 1,000 aqueous benzalkonium (Zephiran) chloride. The Kel-F buttons could be autoclaved.

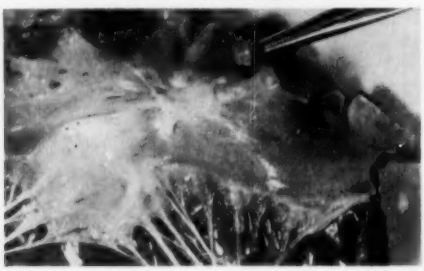

Fig. 5.—Septal defect closed with autologous vein graft examined seven months after operation; left atrial view. The graft is represented by a firm, white contracted mass of scar tissue.

B. Suture Coaptation of Septal Defect Edges.—The maximum-sized defect which could be created in a dog's heart could be closed by simple suture coaptation without excess tension and without tearing out of the sutures. Threads armed with curved Atraumatic needles at each end facilitated the placement of these stitches. Each needle was passed in an upward direction through the septal rim, passing from left atrium into right atrium. Three or four interrupted 0000 Deknatel nonabsorbable surgical (silk) sutures were placed in the defect edges before all sutures were tied to obliterate the orifice.

C. Autologous Free Graft of Peripheral Vein Sutured over the Septal Defect.—Segments of the external jugular vein were excised from the neck, turned inside out so that the endothelial lining was on the outside, and secured to the septum with 10 or 12 sutures of 0000 Deknatel silk, in a manner to cover over the artificially made septal opening.

D. Autologous Free Graft of Pericardium Sutured over the Defect.—An oval segment of pericardium of appropriate size was cut away from the cardiac envelope and was then sutured as a free graft to the cardiac septum with 10 or 12 sutures of 0000 Deknatal silk, in such a way as to cover the septal opening.

E. Autologous Free Graft of Right Atrial Appendage Sutured over the Defect.—The right atrial appendage was amputated; this appendage tip was laid aside in a moist saline sponge. The defect at the base of the atrial appendage was repaired with interrupted 0000 Deknatel silk sutures, and then a rubber "well" was attached to the heart, permitting entry to and manipula-

tion within the right auricle. An interatrial septal defect was created, and this was then closed by fixation over it of the appendage tip, which had been previously procured; this was appropriately placed and anchored to the septum with 5 to 10 interrupted sutures of 0000 Deknatel silk.

F. Homologous Free Graft of Atrial Appendage Sutured into the Defect.—Atrial appendage tissue was removed from donor animals under aseptic precautions. In some experiments, the

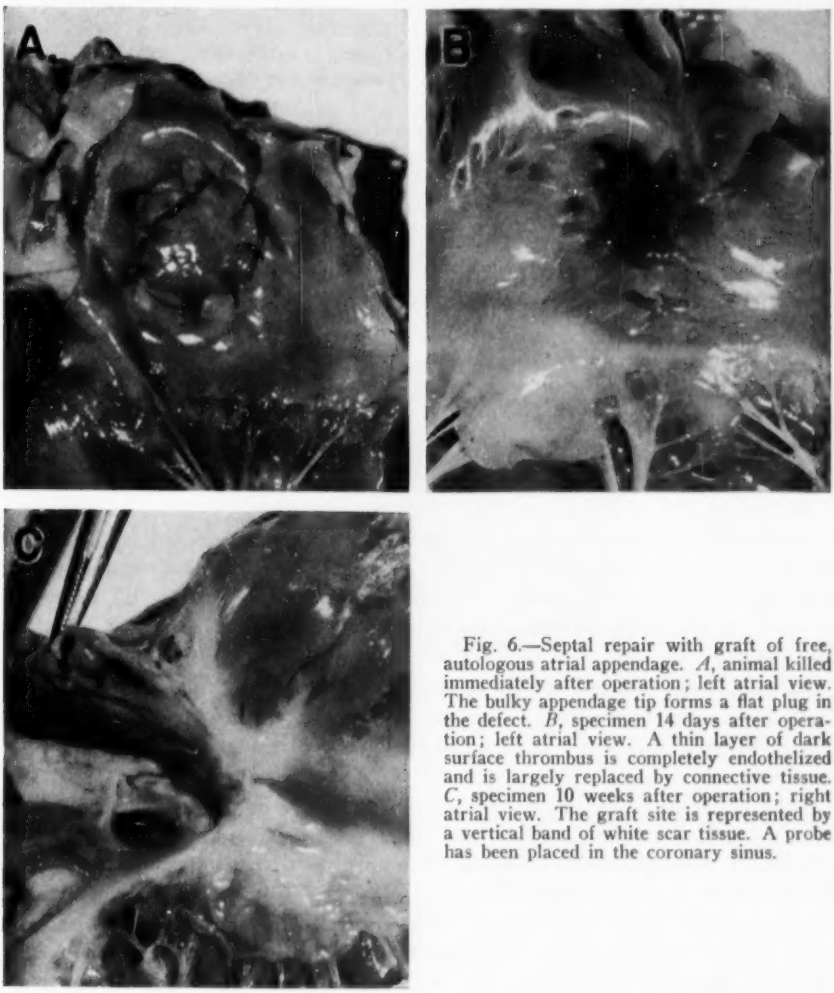

Fig. 6.—Septal repair with graft of free, autologous atrial appendage. *A*, animal killed immediately after operation; left atrial view. The bulky appendage tip forms a flat plug in the defect. *B*, specimen 14 days after operation; left atrial view. A thin layer of dark surface thrombus is completely endothelized and is largely replaced by connective tissue. *C*, specimen 10 weeks after operation; right atrial view. The graft site is represented by a vertical band of white scar tissue. A probe has been placed in the coronary sinus.

tissue was immediately implanted into the defect created in another animal. In other experiments, the appendage tissue was immediately sealed in a sterile polyethylene plastic envelope and stored in a carbon-dioxide ice refrigerator at —55 C. for periods ranging from 3 to 14 weeks. When they were to be implanted into other animals, the grafts were thawed at room temperature prior to removal from the envelope. They were then used for septal repairs, the suturing technique being similar to that used with the homologous atrial appendage grafts.

G. Disc of Rigid Methyl Methacrylate Plastic Sutured over the Defect.—Circular prostheses were machined from rigid methyl methacrylate plastic (2 to 3 mm. thick) and drilled with

multiple holes around the margins (for passage of sutures). The discs were soaked in aqueous solution of benzalkonium chloride 1:1,000 for 24 hours prior to implantation into the experimental septal defects. The appliance was sutured into position with six to eight 0000 Deknatel sutures.

H. Sheets of Pliable Nylon Plastic Sutured over the Defect.—Large sheets of pliable nylon plastic were obtained in 0.13 and 0.81 mm. thicknesses. Ten-centimeter squares of these sheets were sterilized by soaking in aqueous benzalkonium chloride 1:1,000 for at least 24 hours. The small sterile sheet of plastic could be washed with saline and transferred to the operative field and from the sheet; pieces could be cut with scissors to a suitable size and contour to fit the artificially created septal defect. The plastic sheet was sutured to cover the defect with six to eight 0000 Deknatel sutures.

I. Sheets of Pliable Polyethylene Plastic Sutured over the Defect.—Polyethylene sheets in two thicknesses, 0.51 and 1.52 mm., were sterilized in a manner similar to the nylon sheets. Segments of this material could easily be cut with scissors at the operating table and fashioned to proper size and shape. They were placed to cover septal defects and were anchored securely in place with silk stitches.

OBSERVATIONS

Atrial septal defects were treated in 58 dogs. Animals were killed at suitable intervals up to six months. Complete closure was achieved in all but eight animals in which small residual apertures ranging up to 3 or 4 mm. in size resulted from sutures tearing loose or being poorly placed. Microscopic sections were prepared for study.

A. Closure of Defects with Screw-On (Hufnagel) Buttons.—Eight animals were studied. Two were killed immediately after closure of a defect. Other specimens were studied 1, 1, 5, 2, 3, 6, and 12 weeks after operation.

The advantage of using such a button stemmed from the rapidity with which a septal defect could be closed by its use. The entire intracardiac procedure could be completed in a minute or two, a distinct advantage over any of the following methods, in which suture techniques were used and had to be carried out with considerable consumption of time. Practice was required to insert the screw-on prostheses so that they did not shift or twist as they were being joined on the septum. No difficulty was encountered in placing the buttons securely in the experimental lesions where a complete rim of septal tissue was present about the margins of the defect.

The initial tendency was to underestimate the size of the button required to close a defect with surety. The coronary sinus could be avoided easily as a button was placed, but distortion or occlusion of the orifices of the right pulmonary veins was frequently observed with a button of sufficient size to occlude a large experimental lesion. Recognition of the possibility of this error is important, since there is no way of evaluating the position of the button in relation to the structures of the left atrium once the prosthesis has been placed so as to shut off the interatrial hole.

Two animals were killed within 10 minutes after placement of buttons. Each button was already covered by a thin, loosely adherent fibrinous clot over exposed surfaces. In one of these buttons the surface of the plastic presenting into the right atrium had the usual dull machine finish, while the other surface, presenting into the left atrium, had been polished to mirror smoothness with optician's rouge. Covering of the mirrored face with surface thrombus was not complete in 10 minutes.

whereas the side having the machine finish was fully covered. However, the mirrored surface was partially covered in the 10-minute interval, and it is likely that no appreciable differences in late healing processes would have resulted from such minor variations of the plastic surfacing.

In specimens examined late, the thin thrombus capsule was converted to a fibrous capsule between the 6th and the 12th week. Endothelization was completed in two to three weeks.

Although this prosthesis is the bulkiest appliance we have placed in the heart, there was no apparent interference with cardiac function and no evidence of excessive thrombus formation. No difference was apparent in the tissue response to Kel-F as compared with the response to methyl methacrylate.

B. Suture Coaptation of Defect Edges.—Six animals were studied. Tissues were examined 2 and 5 days and 4, 5, 8, 12, and 24 weeks after operation.

It was possible to close by suture coaptation any defect which could be made in the heart of a dog; the maximum-sized defect which could be made did not exceed

Fig. 7.—Photomicrograph of the atrial septum three weeks after defect closure by implantation of free, autologous graft of atrial appendage. The edge of normal septum (marked *1*) is joined to the graft (marked *3*) by a firm scar (marked *2*). The serosal surface of the graft (marked *4*) is covered by a connective tissue layer (marked *5*), over which new endothelium has grown. It is apparent that the serosal surface of the graft does not constitute the late lining of the area of repair. Hematoxylin and eosin stain; × 25.

2.5 cm. in diameter. The openings could be sutured without distortion of the adjacent valve rings and without other apparent interference with cardiac action. Tearing of sutures was not a problem, and in one instance a large defect was closed with interrupted 00000 arterial silk sutures without breakage of the strands.

Tissue repair after suture closure was accomplished by the progression of changes characteristic of primary wound union. In the first specimen, examined two days after operation, there was a complete thin layer of thrombus overlying the suture-coaptation site. At five days, the thrombus was partially organized. The surface of the clot was smooth, and flat endothelial cells could be seen covering its surface. In the specimen examined at four weeks, the suture site had been converted into a thin band of scar tissue. Between 8 and 24 weeks after operation, there was a continuation of the scarring process, with appearance of a collagenous and relatively acellular connective tissue.

(Direct suture of some of the larger septal defects in man might be unsatisfactory because of too much tension on sutures or because of thinness of septal edges.)

C. Autologous Free Graft of External Jugular Vein Sutured into the Defect.— Grafts of external jugular vein (turned inside out) were placed in three animals. Only a few experiments were done, because it soon became apparent that soft venous tissue was unsatisfactory to handle in the operative field. As sutures were placed in the graft, the thin membranous material would become twisted, making it difficult to maintain alignment of a series of sutures. Many stitches were required to fit accurately such a thin tissue graft to the edges of a septal defect. As the sutures were tied, the edges of the membranous graft would become tented, leaving gaps in the interstices between sutures. (In contrast, bulkier atrial appendage grafts, described later, would tend to fill in the space between sutures, so that good defect closure could be obtained with fewer sutures.)

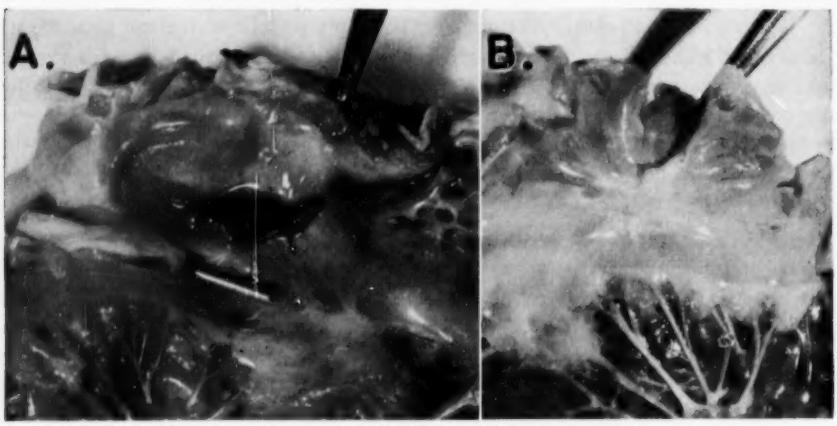

Fig. 8.—Septal repair with graft of frozen, homologous atrial appendage. *A*, 14 days after operation; right atrial view. The graft and all sutures are endothelized. Probe lies in coronary ostium. *B*, specimen three months after operation; left atrial view. Healing is complete. Prior to implantation, this graft had been frozen 40 days at —55 C.

Two specimens were examined the day following their placement. Surface thrombus formation was minimal and occurred as small clots covering sutures and suture knots. In a specimen studied seven months after placement, the region of repair consisted of an irregular hard white scar. One focus of calcium deposition was seen.

D. Autologous Free Graft of Pericardium Sutured into a Defect.— Studies with pericardium were discontinued after implantation of one graft showed that the disadvantages inherent in the membranous vein grafts also prevailed with pericardium. The material was too soft and could not be identified accurately by palpation when one was trying to place it, working by "feel" under a column of blood. The specimen at five months presented changes similar to those described late after jugular vein grafting; there was complete scar closure of the septum.

E. Autologous Free Grafts of Atrial Appendage Sutured into Defects.—The atrial appendage, amputated at its base, presented many desirable characteristics

for use as an intracardiac graft. It was a relatively thick muscular structure and was readily available in the operative field. Its bulk made for ease in handling manually or with instruments, and when suturing was accurately performed, the graft acted as a flat wad of tissue which plugged the hole effectively. These grafts were placed in 10 animals.

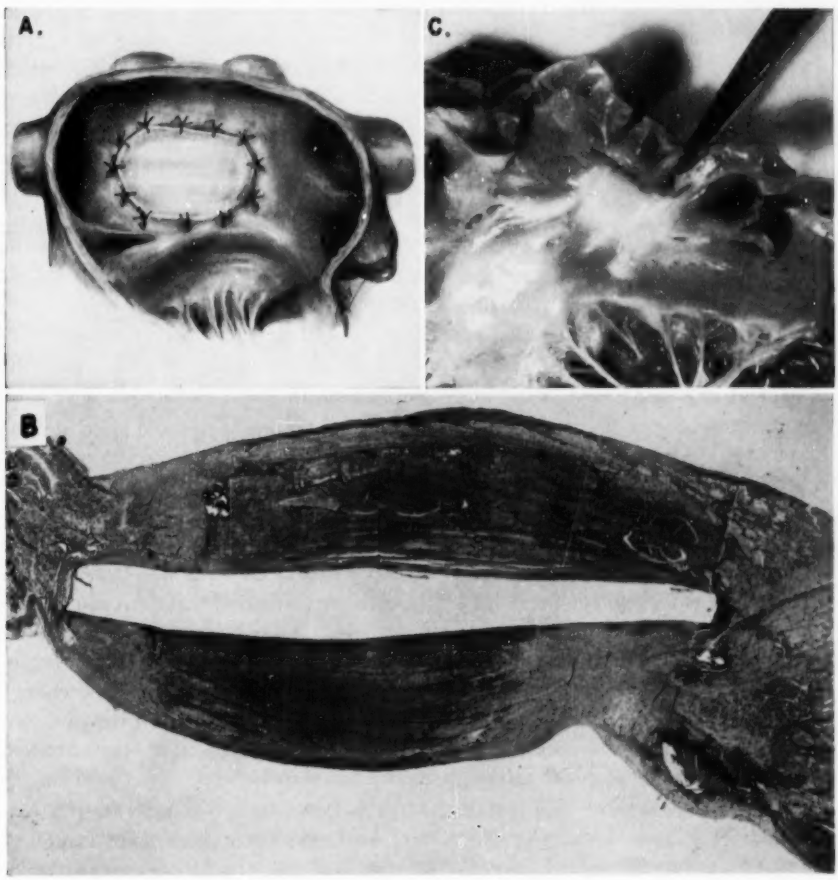

Fig. 9.—Closure of atrial septal defect by suturing into place a piece of pliable polyethylene sheet, 0.5 mm. thick. *A*, drawing showing the polyethylene sheet held in place by silk sutures at its periphery. *B*, photomicrograph of region of polyethylene implantation, two weeks after operation. The foreign material is completely buried. *C*, specimen obtained four months after operation. There is complete fibrous tissue coverage of the plastic film and smooth endothelization of the area.

Specimens were examined one, two, and three weeks and at two, five, three, four, five, six, and eight months after operation. The immediate thrombus formation on the surface of the graft did not exceed 1 mm. in thickness. Endothelization was complete in the first specimen, examined one week after operation, and no con-

clusions can be drawn as to the mode of formation of this endothelial layer. In successive weeks, the endothelial layer thickened slightly and a well-developed subendothelial connective tissue layer was formed. It should be emphasized that this layer of endothelial cells was newly formed over the surface of the encasing thrombus, so that the old endothelial lining of the graft did not constitute the late endothelial lining of the repair region. Since the endothelial surface of such grafts did not constitute the late endothelial membrane of the septal area, it might be concluded that, in the dog, any advantage of using endothelized tissue as a graft derives only from influence on the minimal development of surface thrombus, rather than from any virtue the graft might possess as a persisting endothelized structure.

Amputation of the atrial appendage and separation from its intrinsic blood supply led to loss of viability of the muscle fibers of the graft. One week after operation, this change was manifested by a homogeneous, pale, eosinophilic-staining property of the muscle fibers. The muscle fibers of the graft stained a much lighter pink than the muscle fibers of the adjacent viable septal rim. Muscle striations in the graft were no longer visible, and there was disappearance of the nuclei in the muscle fibers and fibrous stroma. In spite of these changes, there was no tendency to disintegration of the transplanted appendage. Apparently, the structural integrity and position of the grafts were maintained by the encasing thrombus and the remaining tensile strength of the nonviable connective tissue elements.

The nonviable graft tissue was phagocytosed and gradually replaced by connective tissue starting in the granulation tissue margin that appeared between the septal rim and graft. Connective tissue replacement was 90% complete in specimens examined at the end of three weeks and was fully completed at the end of 10 weeks. Three months after operation, there was a decrease in vascularity and cellularity of the connective tissue, with considerable deposition of collagenous substance. In scattered areas throughout the older grafts, collagen formation was extremely dense and consisted of whorls of deeply basophilic fibers similar in structure to elastic cartilage. In grafts examined five months after operation, a number of small calcium deposits were seen. In all specimens the areas of cartilaginous or calcific change were overlain by an intact endothelial surface and well-developed subendothelial layer of connective tissue. There was no evidence of distortion or fragmentation of an intimal membrane over cartilaginous or calcific foci.

F. Homologous Free Grafts of Atrial Appendage.—In two animals fresh homologous free grafts of atrial appendage were implanted; specimens were examined four and six months after operation. In eight animals, frozen homologous atrial appendage grafts were sutured into position and the animals killed at 1, 2, 3, 4, 5, 6, 9, and 12 weeks. The healing pattern observed in both the frozen and the nonfrozen grafts was similar to that noted in the autologous appendage group. Phagocytes and fibrous tissue replacement occurred in the same manner, although the transformation was several weeks later than comparable changes in the autologous grafts. Scattered areas of tissue liquefaction were observed in specimens in the homologous group, so that the final result was a more fatty type of connective tissue.

G. Discs of Rigid Methyl Methacrylate Plastic Sutured over the Defect.—Two animals had defects closed by suture onlay of rigid methyl methacrylate discs, 2 to 3 mm. thick; the specimens were examined two and five weeks later. These rigid

prostheses must be machined before operation to the desired contour; holes must be drilled before operation in the prosthesis margin for passage of sutures. Both these factors are a great disadvantage. Because of the availability of pliable plastic films, which may be easily cut during operation to the exact contour of the defect, rigid discs offered no apparent advantage in septal repairs.

The discs showed a nonreactive response and were rapidly incorporated into the substance of the septum in a manner similar to that described below for polyethylene. At five weeks, there was no evidence of cyst formation or displacement of the rigid disc from its fibrous capsule.

H. Pliable Nylon Plastic Film Sutured over the Defect.—Openings were closed in 14 animals by suture onlay of pliable nylon plastic sheets. The material was easy to work with and to fit into place. Specimens were examined after operation at 4 hours and at 1, 1, 2, 2, 3, 3, 6, 6, 9, 12, 12, 16, and 16 weeks.

The plastic sheets were rapidly covered by a thin layer of surface thrombus, which was organized quickly to form a firm fibrous capsule. Generally, there was a pattern of tissue repair which was similar to the polyethylene sheet response described below, although nylon implantation called forth a severer exudative reaction in the thrombus overlying the plastic material; there was infiltration of numerous polymorphonuclear neutrophiles and a tendency to form sessile polyps of thrombus about the margins of the area of repair. These changes did not interfere with incorporation of the prostheses into the septum but did suggest that our particular lot of nylon was not the plastic of choice. Later, careful investigation of the manufacturing process of this nylon batch revealed that small amounts of formaldehyde may have been liberated during polymerization, and traces of this impurity may account for the greater tissue response which we noted.

I. Pliable Polyethylene Sheet Sutured over the Defect.—In 12 animals, pieces of pliable polyethylene sheeting, 0.5 or 1.5 mm. in thickness, were sutured over the defects. The thinner material was superior in its physical qualities while being placed in the heart. Specimens were examined postoperatively at 1 day and 1, 1, 5, 2, 3, 6, 6, 8, 9, 10, 16, and 18 weeks.

The earliest specimens showed a thin layer of thrombus less than 1 mm. in thickness covering the plastic sheet. This early thrombus was firm and continuous. It was loosely adherent over the main body of the plastic sheet but tightly adherent to the sutures at the periphery of the repair area. Specimens examined one and two weeks after operation revealed slight increase in the thickness of the thrombus, which was completely endothelized. After two weeks, the purple-red thrombus was organized into a tough fibrous membrane. After six weeks, the firm capsule blended smoothly in contour with the adjacent septum. Conversion of the bland thrombus into granulation tissue and fibrous scar was initiated in the subendothelial layers of the thrombus and progressed deeply, so that the layer of thrombus immediately adjacent to the plastic surface showed early signs of organization as late as eight weeks after implantation. Despite this delay in deep organization, there was no tendency to cyst formation about the foreign substance or displacement of the plastic prosthesis. The polyethylene sheet always became an integral part of the atrial septum. (There was no important difference in reactions to the sheetings of different thicknesses.)

COMMENT

The general uniformity of the healing pattern of heart tissue was of particular interest. In spite of variations in the contour and properties of tissue grafts and plastic prostheses, the dog heart was able to ensheath new substances by an adherent thrombus, endothelize this clot, and incorporate the substance into a firm fibrous structure. Regardless of the type of surgical repair, these changes proceeded with only minor variations in the modes of healing. Postoperative healing always has been accomplished without serious propagation of thrombus or embolization. It was apparent in these studies that the most careful attention to detail in repairing the defects accurately was much more important in obtainig good end-results than were the variations in the shape or surface properties of the tissue grafts and plastic prostheses which were studied.

It would appear that the thickness and contour of the encasing surface thrombus was determined as much by contour and positioning of the graft or prosthesis as by the surface properties of tissue grafts or plastics. The contour of the surface thrombus is probably determined by the production of regions of blood stasis or swirling in the atrial chamber. When plastic prostheses were sutured into position, the thrombus was thicker than was a clot over bulky tissue grafts. By virtue of the technique of operation, a plastic prosthesis sutured into position tended to overlie the edge of the defect on the right side of the septum. This left a slight indentation on the left atrial side of the prosthesis which filled in with a thicker thrombus, so that eventually a smooth contour was presented to each atrium.

Endothelization of the surface thrombus was always prompt. In every instance the endothelial lining appeared to be derived from the endothelial margin of the defect rather than from differentiation of endothelium from granulation tissue histiocytes in patchy areas. The endothelial covering of the plastic prosthesis proceeded at a slower rate than endothelization of tissue grafts. There was no correlation between the rate of centripetal growth of the sheets of endothelial cells and the rate of organization of the underlying thrombus.

A criticism might be raised that the smoothly endothelized septal orifice in the human may differ in its healing properties from the freshly created lesions in the dogs which we studied, where a raw edge of muscular tissue was present at the rim of the surgical repair. We have attempted to answer this question in other animals by simply suturing a piece of plastic film onto the surface of an intact atrial septum so that no raw edge of muscular tissue was present in the region of attachment. Under these conditions, a general cellular response is evoked along the entire edge and surface of the plastic, well away from points of suture perforation. The reaction is just as marked as the reaction in animals which have raw septal edges; thrombus formation and endothelization processes are similar. These findings would suggest that the presence of a new substance and surface thrombus in the repair region is the prime factor initiating the cellular response. It is probable that inconsequential variations might be anticipated in the healing mechanisms after closure of smoothly endothelized, naturally occurring formations in man. Consequently, we can see no reason to roughen the edges of a septal orifice in humans with the intention of accelerating the sequences of organization.

The extension of conclusions drawn from animal experiments to human applications must be made with the reservation that there may be species variation in the

rapidity of the clotting mechanism, the healing process, and the rate of endothelization. The greater sensitivity of dogs to endocardial injury has been discussed by Goodale and co-workers.[5] This species difference would suggest that excessive thrombus formation would occur in dogs with the slightest error in operative techniques, but in our experience serious propagation was not found after we had developed dexterity in closing defects accurately through a rubber "well." The slower clotting mechanism in humans might make precise closure of a defect much more important in the human than in th dog, in which spontaneous filling in of small gaps can often be expected. We have demonstrated to our own satisfaction that it is possible to achieve accurate and complete defect closure through the rubber "well." In the last 30 animals of this series, immediate examination of the closure by palpation during operation showed that no significant residual openings had been left, and that there would be no necessity for later bridging of extensive residual defects—bridging which might be more effectively accomplished in the dog than in the human.

Decisions will have to be tentative as to the methods of choice for closure of the natural malformations in humans. Small septal openings can be closed best by simple suture coaptation. We can draw no conclusions as to the upper limit of size for such a method of closure. In our limited experience in humans, we have placed some sort of prosthesis whenever there was the slightest possibility that a defect was too large to be closed by suture without excessive tension. We have thereby avoided the risk of irreparably damaging septal margins in the attempt to see whether suture closure could be effected. The decision not to attempt suture closure has also been governed by other factors, including the location of the orifice in proximity to valve rings and drainage points (pulmonary vein or coronary sinus), which might be occluded by a distorted closure, and the quality of the rim of septal tissue, which may be too thin to tolerate even the slightest amount of tension.

Defects not suitable for suture coaptation can be closed by the addition of some substance to bridge the defect, whether that be invaginated lateral atrial wall, free-tissue graft, or plastic prosthesis. In spite of the excellent healing responses after the implantation of various free-tissue grafts, we have not implanted such tissues when repairing human malformations because tissue grafts are a little more difficult to work with than are the plastics which are now available and which have been shown to be acceptable.

Although screw-on buttons functioned satisfactorily when closing defects which were made in the dog, where a sturdy rim of septal tissue was always present around the entire periphery, we have had them shift out of position in humans when the septal rim was incomplete or was irregular in thickness in its various parts. Consequently, we believe these appliances will seldom prove to be satisfactory for septal closures in human cases.

The minor variations in reaction to plastics of various types and the absence of late complications in animals in which plastics were implanted lead us to believe that these substances are quite acceptable for closing large defects in man. We prefer the pliable polyethylene film of 0.51 mm. thickness. It has physical properties which make it easy to work with at the operating table. It appears to give a little less reaction than does nylon sheeting.

SUMMARY

The necessity for study of many methods of repairing septal defects stems from the variability of interatrial septal orifices which occur in man. These variations in size, shape, and location in the septum indicate that it is desirable to have at hand several different methods for closure of defects as they are approached in humans.

A comparative study has been made of the serial healing patterns in the dog heart following the immediate closure of defects which were created in the atrial septum. Methods of closure subjected to study were (1) repair by means of rigid plastic screw-on buttons; (2) suture coaptation of the defect edges; (3) use of autologous free grafts of pericardium or vein, or use of free grafts of autologous or homologous atrial appendage; (4) closure by suture onlay of rigid plastic discs or of onlay of pliable nylon or polyethylene sheet to cover the defect.

All of the methods of repair in the experimental animal led to a rather uniform pattern of healing by thrombus formation over the region of the closure and by endothelization of the surface of the thrombus. Thrombi were gradually transformed into fibrous scars. Autologous and homologous free-tissue grafts were replaced with fibrous tissue. The foreign materials studied were accepted by the heart in an amazing manner and became an integral part of the septum.

A number of considerations have led us to the conclusion that auricular defects in the human can be closed by simple suture coaptation of smaller openings, whereas very large openings can be repaired well by the onlay of a sheet of plastic material, for which polyethylene film, 0.5 mm. thick, has suitable properties.

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CONGENITAL ATRESIA OF EXTRAHEPATIC BILE DUCTS

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THE PRESENT dissertation is a report of 27 cases of congenital atresia of the extrahepatic biliary tract that have been encountered at The New York Hospital from 1932-1952. Although the condition occurs infrequently, more than 300 cases have been reported in the literature. Moore [22] estimated that there is one case in 20,000 to 30,000 births.

Jaundice in the newborn is not uncommon and may be a manifestation of physiologic icterus neonatorum, erythroblastosis fetalis, septicemia, syphilis, or obstruction of the biliary tract. Primary blood dyscrasias such as Mediterranean, congenital hemolytic, sickle cell, and acute hemolytic anemia are also associated with jaundice but tend to occur later in childhood.

Physiologic icterus neonatorum is common, occurring to some degree in 50 to 75% of all newborn infants,[21] and is manifested by a mild jaundice, appearing on the 2d or 3d day and disappearing usually by the 14th day. The liver is not enlarged. Bile pigments are found in the stool. Erythroblastosis fetalis can be established on the basis of Rh-incompatability in the parents and a Coomb's test on the child's blood. Septicemia may cause icterus of variable degree as a result of hemolysis of red blood cells. However, this is accompanied by high fever, leucocytosis, and other signs of generalized infection. The liver is not usually enlarged, and bile pigments are present in the stool. Syphilitic hepatitis, which may produce mild jaundice, can be determined by means of serologic tests on infant and mother and roentgenograms of long bones of the child.

Jaundice at or shortly after birth which is unremitting and is associated with an enlarged liver, dark urine, acholic stools, and a positive direct van den Bergh reaction of the serum makes the diagnosis of obstruction of the biliary tract probable. Ladd [16] has indicated that in cases of complete obstruction, bile pigments may be found in the stool occasionally, owing to the fact that bile pigments may be excreted into the lumen of the intestine from blood vessels in the mucosa.

However, the diagnosis may be difficult in the first month of life, and Ladd [16] states that if the final diagnosis of congenital obstruction of the biliary tract is delayed until the infant is 1 month or 6 weeks old, the chance of error is not great. This is of practical significance because obstruction of the biliary tract can be established only at time of laparotomy.

Biliary obstruction in infancy may be due to (1) mechanical blocking secondary to inspissated mucous or bile plugs, inflammatory reaction about ducts or the ampulla of Vater, stones or extrinsic pressure on the biliary tree; (2) congenital malforma-

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tions of the biliary tract. The commonest cause of obstructive neonatal jaundice is congenital atresia of extrahepatic bile ducts.[22] The conditions causing mechanical blocking give rise in most instances to a picture similar to that caused by congenital malformations, and differentiation can be made usually at operation only. In the present paper attention will be focused on congenital malformations that cause biliary obstruction.

Review of the literature on this subject reveals that many types of malformation may occur. Several authors * have attempted to classify the cases in broad general groups. Those in which the gall bladder and/or cystic duct only are anomalous or absent are of no clinical significance since they do not give rise to jaundice. Omitting these, a simple classification of congenital malformations of the extrahepatic biliary ducts can be given as follows:

I. Complete agenesis of extrahepatic ducts

II. Complete or partial atresia of either hepatic duct or common hepatic duct
  (*a*) with atresia of cystic duct
  (*b*) without atresia of cystic duct

III. Complete or partial atresia of common bile duct
  (*a*) with atresia of cystic duct
  (*b*) without atresia of cystic duct

TABLE 1.—*Onset of Jaundice*

Time	No. Patients
At birth	8
Birth-2 wk.	11
2-4 wk.	1
1-2 mo.	4
2-4 mo.	1
4-6 mo.	1
6-12 mo.	1

Although case reports had appeared earlier, the first review of the subject was by Thomson [28] (1891) who discussed 50 cases. Subsequent reviews by Beneke [4] (1903), Flebbe [8] (1907), Holmes [13] (1916), Ladd † (1928-1935), Donovan [6] (1937), Stolkind [26] (1939), Gerrish and Cole [9] (1951), Moore [22] (1953), and Gross [11] (1953) have added to the total number of cases available for analysis. In addition to these larger series, occasional reports of smaller groups have been recorded in both English and foreign literature. Several of the cases cited by earlier workers included anomalies of the extrahepatic biliary system which are not associated with icterus. They were usually found at necropsy and were not the cause of death.

Embryologically, the liver and its ducts arise from a ventral outgrowth from the floor of the future duodenum. This consists of a cranial portion that will differentiate into the glandular tissue and intrahepatic bile ducts and a caudal portion that becomes the gall bladder and cystic duct.

The main portion of the hepatic diverticulum elongates into the ductus choledochus and hepatic duct. The bile ducts within the liver, which are tributary to the hepatic duct, arise in a secondary manner, beginning at eight weeks.

* References 12 and 16.
† References 15 and 16.

TABLE 2.—*Patients with Extrahepatic Bile Duct Atresia*

Case and History, No.	Age, and Yr.	Sex and Color	Age at Onset of Jaundice	Anomaly	Proved at			Amenable to Surgery		Operation	Result	Age at Death	Comments
					Operation	Autopsy	Both	Yes	No				
1 (64186)	2 mo. 1934	M W	8 days	Atresia of all extrahepatic bile ducts	..	..	+	....	No	Cholecystostomy	Died 3 days p. o.	2 mo.	Gall bladder contained no bile
2 (149838)	2 mo. 1937	F W	Birth	Common bile and hepatic ducts obliterated	+	..	..	....	No	Exploration	Unknown	Unknown	No follow-up
3 (166405)	16 mo. 1937	F W	Birth	Atresia of common bile and cystic ducts	..	..	+	Yes	...	(1) Drainage of hepatic duct, 1937 (2) Hepatic duct-duodenostomy, 1938	Fair Died p. o.	..... 25 mo.	Did well for 9 mo. after first operation
4 (172482)	2 mo. 1937	F W	2 wk.	Common bile duct atresia	..	+	..	Yes	...	None	Died 2 days after admission	2 mo.	Died before operation could be performed
5 (128628)	5 mo. 1940	M W	Birth	Atresia of all extrahepatic bile ducts; gall bladder absent	..	+	..	....	No	None	Died 3 days after admission	5 mo.	.....
6* (289988)	4 days 1941	F W	1 day	Fine stricture of common bile duct near duodenum	+	..	..	Yes	...	Cholecystostomy	Good*	Living	No evidence of biliary-tract disease, but has cerebral palsy
7 (301452)	7 mo. 1941	F W	5 wk.	Extrahepatic bile ducts not identifiable	+	..	..	....	No	Exploration	Died 9 mo. p. o.	16 mo.	Died in coma; no autopsy
8 (304062)	10 days 1941	F W	3-5 days	Common bile duct absent	..	..	+	Yes	...	T-tube drainage of common bile duct	Did well for about 11 mo.; readmitted because of jaundice, light stools, dark urine; died 1 day after 2d admission	1 yr.	Choledochal duodenal fistula formed after operation; jaundice apparently recurred from inflammatory narrowing of fistula and cholangitis
9 (331516)	2½ yr. 1942	F W	3 wk.	Atresia distal ½ common bile duct	+	..	..	Yes	...	Choledochoduodenostomy	Excellent	Living	Last follow-up 4/51, no jaundice, enlarged liver, symptoms, or signs
10 (341516)	2½ mo. 1942	F W	Birth	Extrahepatic bile ducts not identifiable; gall bladder absent	+	..	..	....	No	Exploration	Died 5 wk. p. o.	3½-4 mo.	No autopsy
11 (413718)	7 mo. 1945	M W	6 mo.	Common bile duct not identifiable	+	..	..	Yes	...	Cholecystoduodenostomy	Died 4 days p. o.	7 mo.	Had massive rectal hemorrhage and died 4 days p. o.; no autopsy
12 (431350)	7½ wk. 1946	F W	5½ wk.	Right, left, and common hepatic ducts atrophic	+	..	..	....	No	(1) Exploration (2) Exploration, 1946; splenectomy, 1950	Readmitted 1947, 1949, for jaundice; 1950, splenomegaly	Living	Follow-up 10/52: hemangiomata, liver 3-4 cm. below RCM; no jaundice; general condition good
13 (468475)	5½ mo. 1947	F W	Birth	Hepatic, common bile, and cystic duct absent	..	..	+	....	No	Exploration	Died 1 yr. p. o. (at another hospital)	17½ mo.	No intrahepatic duct tissue on autopsy
14 (482513)	7 days 1947	F W	6 days	Common bile duct atresia	..	..	+	Yes	...	Exploration	Died 4 hr. p. o.	32 days	.....
15 (489753)	3 mo. 1947	M W	9 days	Atresia of hepatic, common bile, and cystic ducts	..	..	+	....	No	(1) Exploration (10/47) (2) Hepatojejunostomy (11/47)	Died 8 days p. o.	4-4½ mo.	Multiple liver abscesses on autopsy

16 (491264)	6 mo. 1947	M W	3-4 days	Atresia of all extrahepatic bile ducts; gall bladder absent	+	..	..	....	No	Hepatojejunostomy Jejunojejunostomy	Fair	Living	Last seen 12/52; jaundice; liver and spleen enlarged, dilated thoracoabdominal veins
17 (488533)	7 wk. 1947	F W	5 wk.	Atresia of all extrahepatic bile ducts	+	..	..	....	No	Hepatojejunostomy	Poor	Unknown	No follow-up since 1950
18 (493466)	6 wk. 1947	F W	Birth	Atresia of all extrahepatic bile ducts	+	..	..	....	No	Hepatojejunostomy Jejunojejunostomy	Good, immed. p. o.	Unknown	No follow-up since 1948
19 (506660)	5 wk. 1948	M W	2 days	Atresia of all extrahepatic bile ducts	..	..	+	....	No	Cholecystostomy	Poor; died 7 mo. p. o.	8½ mo.	.....
20 (529118)	11 mo. 1949	F Chinese	3 mo.	No extrahepatic bile ducts identifiable	+	..	..	....	No	Exploration	Died at home shortly after discharge	Approx. 13-14 mo.	Hepatojejunostomy at time of exploration not done owing to lack of flow of bile from cut edge of liver
21 (544557)	11 mo. 1949	F W	Birth	Atresia of all extrahepatic bile ducts	+	..	..	....	No	(Exploration at another hospital, 2 mo. of age) Explored NYH 14 mo. of age	Died 2-3 wk. p. o.	14½-15 mo.	No autopsy (died about 1 yr. after original exploration)
22 (584242)	7 mo. 1950	F W	1 mo.	Agenesis distal ⅓ of common bile duct	..	+	..	Yes	...	None	Died 19 days after admission	7½ mo.	Ascites, varices present on admission
23 (601557)	7½ yr 1951	M W	1 yr.	Agenesis distal ⅓ of common bile duct	+	..	..	Yes	...	(1) Cholecystojejunostomy and jejunojejunostomy (age 5½ yr.) at another hospital (2) Cholecystostomy	Unsuccessful; died 11 days p. o.	7½ yr.	Temperature spikes, light stools, dark urine after 1st operation; developed bleeding tendency and had 2 convulsions; died p. o. 11 days (2d operation); no autopsy
24 (614902)	1½ yr. 1951	M W	3 days	No extrahepatic bile ducts identifiable	+	..	..	....	No	None at NYH (exploration, at another hospital, age 4 mo.)	Died 15 days after admission (14½ mo. p. o.)	1½ yr.	No autopsy; had developed ascites 5 mo. before admission; jaundice progressed
25 (609810)	7 wk. 1951	F W	Birth	Right, left and common hepatic ducts obliterated	+	..	..	....	No	Hepatojejunostomy and Roux Y	Poor immediate p. o. course; developed heart failure; gradual improvement	Living	Since discharge has had good appetite, weight gain; stools, urine unremarkable; no edema, jaundice, pruritus, ascites
26 (628975)	24 days 1952	M W	3 days	"No evidence of extrahepatic biliary system"	+	..	..	....	No	Hepatojejunostomy and Roux Y	Fair	Living	Occasional brown stools; stools occasional 3-4 + guaiac; negative for guaiac and bile when last seen (12/52)
27 (635212)	5½ yr. 1952	M W	3 days	Common bile duct and cystic duct absent	+	..	..	Yes	...	(1) Exploration at age 8 days; common bile duct absent (2) Exploration and attaching "small bile duct to intestine" at age 4½ yr.	Poor Poor to fair	Living	Ascites; liver 3 to 4 cm. below RCM; small umbil. hernia, dilated thoracoabdominal veins, occasional melena (to be considered for further surgery at time when all records are available)
Totals:					17	3	7						

* On basis of subsequent course this patient probably had inspissated bile or a stricture which later became patent.

Note: Jaundice occurred as early as birth to as late as 1 year of age (601557).

Summary: 10 males (37%), 17 females (63%); 26 white, 1 Chinese; youngest 4 days, oldest 5½ yr., average 10 mo. Spread: Birth to 6 mo., 17; 6 to 12 mo., 4; 1 to 2 yr., 3; 2 to 6 yr., 3.

The gall bladder constitutes a separate caudal region of the originally shallow ventral outgrowth. In a 5-mm. embryo, it is a solid cylinder which is carried away from the duodenum by the elongating common duct. A distinct stem, or cystic duct, is then recognizable, and in the seventh week a lumen has been established from the main biliary passage. Bile is secreted in fetuses about 3 months old.[3]

Although many writers have attempted to explain the occurrence of extrahepatic biliary tract atresia, the etiology is still not fully established. The concept of the atresia being due to syphilis, inflammatory lesions of the ducts, or fetal peritonitis [28] have been generally rejected.

Shelton and Torey [25] (1945) suggested that icterus gravis neonatorum might be the forerunner of congenital obliteration of the bile ducts. The mechanism proposed was that of viscid bile occluding the ducts, with subsequent conversion of the ducts to fibrous cords.

Rolleston and Hayne [24] (1901) proposed that "toxins" carried across the placenta might cause injury to the fetal liver, with the development of cirrhosis followed by descending cholangitis and subsequent obliteration of the bile ducts. More recently Ahrens, Harris, and MacMahon [1] (1951) renewed interest in this concept by suggesting that viral hepatitis, which might be quiescent in the mother, could cause liver damage in the fetus, with subsequent descending cholangitis and bile duct atresia. It is their opinion that this concept warrants further investigation.

The most widely accepted etiological theory at present is that proposed by Ylppö [31] (1913). This investigator pointed out that the extrahepatic bile ducts are patent in early fetal life. Later, because of epithelial concresence the lumina disappear, to become patent again further in development. However, in some instances there is an arrest of development during this stage of epithelial concrescence which gives rise to congenital biliary atresia.

REVIEW OF THE NEW YORK HOSPITAL CASES

During the period from 1932 to 1952, we encountered 27 cases of anomalies of the extrahepatic biliary tract that caused definite signs or symptoms of biliary obstruction. The diagnosis was confirmed at operation in 17 cases, at necropsy in 3 cases, and at operation and necropsy in 7 cases. In four cases, the diagnosis had been previously made at operation in some other hospital prior to admission to this institution.

The ages of the patients when diagnosis was first made ranged from 4 days to 1 year. Cardinal signs consisted of jaundice, acholic stools, and dark urine. Later in the course, ascites, edema, prominent thoracoabdominal veins and upper gastrointestinal bleeding, presumably from varices, frequently occurred. Jaundice was usually the first sign noted by the parents. This was apparent at birth in eight cases. The time at which icterus was noted in all cases is indicated in Table 1.

Twenty-six of the patients were white; one patient was Chinese. Although jaundice appeared in all cases before 1 year of age, one patient who had been icteric since the age of 1 year was not seen until he was 5½ years old. At this time, exploration was done at another hospital, and he was found to have common bile duct atresia.

The average age of the patients when seen at the New York Hospital was 10 months. A summary of these cases is presented in Table 2.

Seventeen (63%) of the patients were females and 10 (37%) were males.

Twenty-four patients (89%) were subjected to operation. Four had operations at some other institution prior to admission to the New York Hospital. The types of operations and results are summarized in Table 3.

TABLE 3.—*Types of Operative Procedures and Results*

Operative Procedure	P. O. Deaths, No.	Recoveries, No.	Summary of Results
I. Exploration only			
(a) at NYH	1	7	Died 4 hr. p. o. (1) No follow-up (1) Still living with some liver damage, no ascites, jaundice, 6½ yr. p. o. (1) Died 2-3 wk. to 1 yr. p. o. (5)
(b) at another hospital	0	1	Died 14½ mo. p. o.
II. Cholecystostomy	2	2	Died 3 days p. o. (1) Died 11 days p. o. (1); patient had had cholecystojejunostomy and jejunojejunostomy prior to this operation Died 7 mo. p. o. (1) Living without symptoms of biliary obstruction but has cerebral palsy (1)
III. No operation	3	0	Died 2 to 19 days after admission
IV. Hepatojejunostomy with jejunojejunostomy or Roux Y	0	4	Good immediate course p. o.; no follow-up since 1948—1 yr. (1) Living (3): 2 have jaundice; 1 no signs or symptoms of liver or biliary tract disease
V. Hepatojejunostomy	1	1	Died 8 days p. o.; had multiple liver abscesses (1) Poor p. o. result; no follow-up since 1950, 3 yr. p. o. (1)
VI. Hepatic duct-duodenostomy	1	0	Had had hepatic duct drainage 9 mo. before 2d operation
VII. Choledochoduodenostomy	0	1	Living in good health; no symptoms or signs of liver disease; last follow-up 9 yr. p. o.
VIII. Cholecyst-duodenostomy	1	0	Died 4 days p. o.; massive rectal hemorrhage
IX. Cholecyst-jejunostomy with jejunojejunostomy	0	1	Patient had this at another hospital; died following cholecystostomy at NYH 2 yr. later (Table 2)
X. Common bile duct drainage with T-tube	0	1	Did well for 11 mo. p. o.; signs of obstruction then recurred; patient died 1 day after 2d admission at age 1 yr.
XI. Unknown	0	1	Living, has ascites, enlarged liver, occasional melena (had exploration, 8 days, and [?] anastomosis of biliary tract to intestine, age 4½ yr.) present age 5½ yr.

TABLE 4.—*Incidence of "Correctability" in Cases of Congenital Biliary Atresia*

Author	Date	Cases, No.	"Correctable," No.	Incidence of "Correctability," %
Holmes [13]	1916	145	23	16
Donovan [6]	1937	11	1	9
Ladd and Gross [17]	1941	45	9	20
Amberg and Zuschlag [2]	1944	18	0	0
Gray, DuShane and Henegar [10]	1948	13	2	15
Leyva and Madigan [18]	1948	18	9	50
Strauss [27]	1951	49	17	35
Gerrish and Cole [9]	1951	25	1	4
Moore [22]	1952	31	8	26
Gross [11]	1953	146	27	18
Redo	1953	27	10	37

Surgical correction of congenital atresia of the extrahepatic biliary tract consists essentially in being able to anastomose some portion of the extrahepatic ducts to the gastrointestinal tract, thereby creating biliary drainage from liver to alimentary

canal. When the extrahepatic biliary ductal system is not patent, direct anastomosis of the gastrointestinal tract to the cut edge of the liver has been performed. Such cases, however, have not been included as amenable to operation. In this series, 10 cases (37%) were considered as suitable for surgical correction and 17 cases (63%) were not. Corrective measures were considered possible in some of the larger series in 0 to 50% of cases (Table 4).

Nine (33%) of the patients in the present series were living two months to nine and three-fourths years postoperatively (Table 5).

TABLE 5.—*Status of Patients Who Have Survived Corrective Surgery*

	History No.	Age	Sex	Color	Age at Onset of Jaundice	Operation	Time P. O.	Condition and Result
1.	331516	2½ yr.	F	W	3 wk.	Choledochoduodenostomy	8 yr.	Last seen 4/51, condition excellent; no signs or symptoms of obstruction
2.	491264	6 mo.	M	W	Few days of life	Hepatojejunostomy and jejunojejunostomy	5 yr.	Fair; bleeding tendency; jaundice waxes and wanes; liver and spleen enlarged; dilated thoracoabdominal veins
3.	626975	24 days	M	W	3 days	Hepatojejunostomy and Roux Y	7½ mo.	Fair; occasional brown stools; occasional melena, jaundice
4.	609810	7 wk.	F	W	Birth	Hepatojejunostomy and Roux Y	2 mo.	Poor; ascites; jaundice, compensated heart failure; dilated thoracoabdominal veins
5.	635212	5½ yr.	M	W	3 days	(1) Exploration (2) Splenectomy (3) ? Anastomosis of biliary system to intestinal tract	5½ yr. 2 yr. 1 yr.	Icteric; ascites present; enlarged liver; xanthoma tuberosum; occasional melena; stools occasionally brown; blood chemistries show minimal liver damage
6.	289988*	4 days	F	W	1 day	Cholecystostomy	9¾ yr.	No symptoms or signs of biliary obstruction; mental retardation and cerebral palsy not related to biliary atresia
7.	431350	5½ wk.	F	W	5½ wk.	(1) Exploration (2) Exploration—1946 (3) Splenectomy—1950	6 11/12 yr. 2 yr.	Fair; liver and spleen enlarged; spider hemangiomata present; no varices, ascites, or jaundice
8.	488533	7 wk.	F	W	5 wk.	Hepatojejunostomy	32 mo.	Jaundice persistent, required occasional transfusion; ascites, required occasional paracenteses (not seen since 1950)
9.	493466	6 wk.	F	W	Birth	Hepatojejunostomy and jejunojejunostomy	2 mo.	Decrease in jaundice; bile in stool; none in urine (not seen since 1948)

* On basis of history and subsequent course, this patient probably had inspissated bile or a stricture which later became patent.

PATHOLOGY

Microscopic sections of the liver were available for pathologic examination in 17 of the 27 cases (63%). Ten of these were obtained from autopsy specimens, and the remaining 7 were from biopsy specimens obtained at operation.

In most cases, the liver parenchyma was composed of nodules of hepatic cells separated from one another by broad bands of fibrous tissue containing proliferating bile ducts.

Many hepatic cells contained bile pigments in their cytoplasm, and frequently bile canaliculi were filled with pigment. In some sections areas of necrosis were apparent.

Autopsy in one patient who died at another hospital revealed an absence of the intrahepatic bile ducts. This was the only patient in whom obliteration of the intrahepatic as well as the extrahepatic ducts was demonstrated.

ANALYSIS OF CASES

In the present series of New York Hospital cases, eight patients with conditions not suitable for surgical correction lived from 14 months to six years. Two of them

survived two and one-half and five and one-half years, respectively. Each had hepatojejunostomy performed in an attempt to ameliorate the condition. Two patients are still living at 5½ and 6½ years of age. Liver function is declining progressively, and hepatosplenomegaly and spider angiomata are present in the patient who has survived longest.

Patients who had anomalies which could be corrected were treated by several types of operative procedures (Table 3). Despite the corrective measures, bleeding tendencies, recurrent jaundice, hepatosplenomegaly, dilated thoracoabdominal veins, ascites, and spider hemangiomata have been noted in these cases.

Some of the problems in management are illustrated by the following cases.

REPORT OF CASES

CASE 6 (Table 2).—This 4-day-old white girl had the onset of jaundice at 1 day of age and at operation was found to have stricture of common bile duct close to its entrance into the duodenum. Simple cholecystostomy was performed for decompression, and more definitive surgery was planned for the future. However, the patient's condition improved, and symptoms and signs of liver or biliary-tract disease disappeared without further surgery. Unfortunately, the patient has mental retardation and cerebral palsy, unrelated to her original biliary-tract atresia. The benign course following cholecystostomy suggests that this patient may not have had a true stricture. She was last seen (1951) nine and three-fourths years after operation and has remained free of icterus and evidence of liver disease.

CASE 12 (Table 2).—This 7½-week-old white girl developed jaundice at 5½ weeks of life. Three weeks later, exploration revealed patent extrahepatic ducts, and it was felt that obstructive signs were secondary to inspissated bile. Cholecystostomy was performed. Because icterus persisted, she was subjected to laparotomy again two months later. At this time, atrophic right, left, and common hepatic ducts with patent cystic and common bile ducts were noted. Biliary cirrhosis was also apparent. The child was discharged unimproved. About four years after her initial operation, she was again subjected to exploratory laparotomy because of a decrease in the size of the liver and increasing splenomegaly. The gall bladder was full, emptied on pressure, and appeared unremarkable. The remainder of the biliary tract was not explored. Portal pressure was not significantly elevated. Splenectomy was performed. This organ showed changes consistent with chronic passive congestion. Biopsy of the liver revealed Laennec's cirrhosis. Since this last operation there has been some improvement. Her stools have been brown and her urine light-colored. When last seen (six years 11 months since first operation), she had enlarged liver and spider hemangiomata. There were no icterus, varices, or enlarged thoracoabdominal veins. In the presence of brown stools and light urine, there is reason to question the diagnosis of extrahepatic bile duct atresia made at the time of second exploration.

CASE 9 (Table 2).—The best result was obtained in a 2½-month-old white girl, who at operation was found to have atresia of the distal one-third of the common bile duct, cystic duct, and proximal portion of the gall bladder. Choledochoduodenostomy was performed. Eight years after operation her condition remains excellent, and there are no signs or symptoms of biliary-tract obstruction or infection.

Of the nine patients who have had attempts made at surgical correction, and survived the procedure, two were lost to follow-up. Of the remaining seven, only two are considered to have had a satisfactory result. In one of these the diagnosis of atresia has been questioned because the signs of biliary obstruction disappeared after cholecystostomy and did not reappear despite the fact that further corrective surgery was not performed. The number of cases is too small to permit correlation of the type of procedure with the end-result. It was noted that the most satisfactory result was obtained in the child in whom a choledochoduodenostomy was accomplished.

It is easier to establish continuity of the extrahepatic biliary system with the gastrointestinal tract if the obstruction is in the distal portion of the common bile duct. The reviews of other authors appear to substantiate this view.[10]

COMMENT

Patients with congenital malformations of the extrahepatic biliary ducts that cause obstruction of the flow of bile into the intestinal tract have a poor prognosis. Anomalies which cannot be corrected by surgical intervention usually result in death during the first year of life. Ladd [16] reported that in 20 patients in whom exploration was done and who were found to have noncorrectable conditions the average duration of life was five and a half months. Donovan [6] described the course of inoperable cases as one of progressive decline, with increasing jaundice and constantly enlarging liver and spleen, followed by death at six months. However, several authors have cited patients who lived more than a year without corrective surgery.‡

Ladd [15] reported the first successful surgical correction of atresia of biliary tract in 1928. Gray, DuShane, and Henegar [19] (1948) were able to collect 15 cases in which successful surgical treatment was performed and added 2 cases of their own. Four of these children had cholecystoduodenostomy; seven had cholecystogastrostomy; three had choledochoduodenostomy, and three had hepaticoduodenostomy.

More recently Moore,[22] in reporting on 31 cases of extrahepatic biliary atresia, found only 8 of the patients to have anomalies that could be corrected. However, only one of these children recovered, with an "excellent chance for continued survival and good health as the result of surgical relief of biliary obstruction."

Gross [11] (1953) stated that permanent cures were obtained in 26% of 198 patients treated medically and surgically.

Review of the literature and the analysis of New York Hospital cases indicate that the prognosis depends on the level of extrahepatic biliary atresia and the age at which operation is performed. If atresia or agenesis is close to the liver, prognosis is less favorable than in those cases in which the stricture occurs in the common bile duct. Patients with atresia or agenesis of the hepatic ducts who were previously considered to have anomalies that could not be corrected by surgical methods might benefit by intrahepatic cholangiojejunostomy, as described by Longmire and Sanford,§ if there is a true continuity of the intrahepatic biliary system.

Operations should be performed when the presumptive diagnosis of biliary-tract obstruction has been made. The majority of cases in which successful corrective surgery has been performed has been in patients under 3 months of age. In the New York Hospital group, seven of the nine children in whom operation was beneficial were under 2 months of age. However, one patient, 5½ years old, had had no corrective procedure until the age of 4½ years. He had had exploration on the eighth day of life, which failed to reveal cystic or common bile ducts. After this, icterus persisted, and he gradually developed signs of gastrointestinal bleeding which led to splenectomy at 3½ years of age. When he was 4½ years old, an exploration was done again and some type of corrective surgery was performed (the exact nature of which could not be determined, owing to inaccessibility of another hospital's records). This child also has xanthoma tuberosum. Ahrens, Harris, and MacMahon [1]

‡ References 16, 26, 2, 5, 29, 30, and 7.

§ References 19 and 20.

stated that xanthomatosis occurs only when serum lipid elevation is severe and prolonged. In congenital extrahepatic biliary atresia, the development of biliary cirrhosis and hepatic insufficiency is rapid, causing early death. Thus, xanthomatosis is not expected. In 13 cases of intrahepatic bile duct atresia reported by Ahrens, Harris, and MacMahon,[1] 10 had associated bile duct atresia. In four of the cases reviewed, the patients lived to 3 or 3½ years of age. One other patient was still living at the age of 5. In the majority of patients with intrahepatic bile duct atresia who survived more than three years, skin xanthomatosis was present. Apparently, if there is associated intrahepatic duct atresia, patients with extrahepatic duct atresia have a longer life expectancy. This child may have both intrahepatic and extrahepatic biliary duct atresia.

The other patient who was successfully operated on after the third month of life was a 6-month-old white boy who has lived five years since surgery. He has intermittent jaundice, hepatosplenomegaly, dilated thoracoabdominal veins, and a bleeding tendency. However, this child had a "noncorrectable" condition that was treated by hepatojejunostomy and jejunojejunostomy, with slight improvement.

It seems reasonable to conclude that the longer operation is delayed the more damaged the liver will be, and that, therefore, the greatest chance for success occurs in those operated upon before severe liver damage has occurred.

The present series contains no Negro children, but this is not to be interpreted as evidence that extrahepatic biliary atresia does not occur in Negroes. Although Gerrish and Cole [9] reported they were unable to find any cases of congenital atresia of the biliary tract in Negroes, several authors || have reported such instances. The New York Hospital cases include one Chinese girl with biliary atresia. Thus race or color should not influence the diagnosis or the therapy.

The prognosis for children with extrahepatic biliary atresia is not good. Those who have anomalies that can be corrected by surgical methods have the best opportunity for a favorable result if operation is performed early.

Those with anomalies hitherto not amenable to surgery may be offered some degree of correction by intrahepatic cholangiojejunostomy or by Roux Y hepatojejunostomy.

SUMMARY AND CONCLUSIONS

Twenty-seven cases of congenital atresia of the extrahepatic bile ducts encountered at the New York Hospital from 1932-1952 are reported.

The diagnosis is difficult to make in the first 4 to 6 weeks of life and can be made at operation only. Cardinal signs are unremitting jaundice, acholic stools, and dark urine.

Ten patients (37%) had conditions amenable to surgery. Nine (33%) of these were alive two months to nine and three-fourths years postoperatively. Only two (7%), however, became symptom-free.

The average age of patients on admission to the hospital was 10 months. Six patients were over one year of age when first seen.

The average life span in patients with anomalies not amenable to surgery was 10 months.

The results of the surgical management of the extrahepatic biliary atresia are summarized.

|| References 14, 6, 23, and 22.

Sections of the liver were available for study in 17 (63%) of the 27 cases, and biliary cirrhosis was the characteristic finding. In only one case was there intrahepatic as well as extrahepatic bile duct atresia.

The embryology of the liver and biliary system is briefly reviewed, and etiological theories of congenital biliary atresia are discussed.

Children with obliteration of the extrahepatic biliary system have a poor prognosis, dying usually before the first year of life as a result of increasing liver damage due to bile obstruction.

Surgical correction is possible if there is a patent extrahepatic channel which can be anastomosed to the gastrointestinal tract. Some degree of correction may be offered by intrahepatic cholangiojejunostomy or by Roux Y hepatojejunostomy in cases of complete extrahepatic biliary duct atresia.

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Scientific Exhibits

BENIGN LESIONS OF ESOPHAGUS: SURGICAL SIGNIFICANCE

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GEORGE GREGORY, M.D.
LOS ANGELES

AN ANALYSIS is made of 76 cases of benign lesions of the esophagus. They include leukoplakia, bronchoesophageal fistula, spontaneous perforation of esophagus, esophageal stenosis, esophagitis, and peptic ulcer of the esophagus. The clinical and diagnostic features in this group are stressed, and the results of treatment are reported.

Benign Lesions of the Esophagus present practical problems of Diagnosis and Treatment

•

LEUKOPLAKIA, SUSPECTED OF BEING A PRECANCEROUS LESION, RARELY IS RECOGNIZED CLINICALLY

•

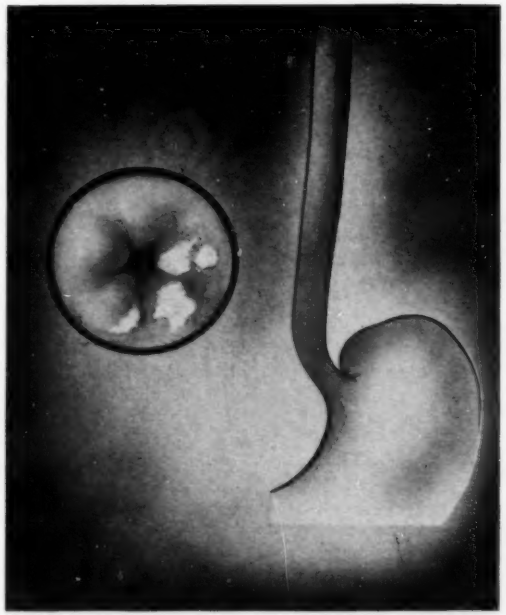
BRONCHO-ESOPHAGEAL FISTULA, SPONTANEOUS PERFORATION AND BENIGN STENOSIS OF THE ESOPHAGUS ARE SATISFACTORILY TREATED BY SURGICAL MEANS

•

ESOPHAGITIS AND PEPTIC ULCER OF THE ESOPHAGUS MAY PRESENT BOTH — DIAGNOSTIC AND THERAPEUTIC PROBLEMS

Chart 1.—As in pathologic conditions of other regions, diagnostic and surgical procedures developed originally for the treatment of malignant disease now are being applied to benign conditions of the esophagus.

Shown as a scientific exhibit of the Section on Surgery, General and Abdominal, at the 103rd Annual Meeting of the American Medical Association, San Francisco, June 21-25, 1954.



CASES 18

DISCOVERED AT AUTOPSY 16

CLINICAL CASES_ 2

♂ 58yrs.

- HISTORY: GASTROSTOMY FOR ESOPHAGEAL STRICTURE OF UNKNOWN ORIGIN 14 YEARS PREVIOUSLY
- TREATMENT: ESOPHAGECTOMY WITH ESOPHAGOGASTROSTOMY
- PATHOLOGIC REPORT: ATRESIA OF ESOPHAGUS WITH LEUKOPLAKIA
- RESULT: SATISFACTORY

LEUKOPLAKIA

MAY BE SYMPTOMATIC OR ASYMPTOMATIC

A FREQUENT FINDING AT AUTOPSY

♂ 69 yrs.

- HISTORY: DYSPHAGIA AND REGURGITATION FOR 2 MONTHS
- X-RAY: OBSTRUCTION DISTAL ESOPHAGUS

  ESOPHAGOSCOPY WITH BIOPSY: LEUKOPLAKIA
- TREATMENT: CONSERVATIVE
- RESULT: IMPROVED

LEUKOPLAKIA

Chart 2.—Leukoplakia of the esophagus is included because it is so frequently found at autopsy and so rarely is it diagnosed clinically. Of the 18 cases collected, only 2 were diagnosed clinically. To the clinical cases, both conservative and surgical forms of treatment were applied, with satisfactory results in both instances.

BRONCHO-ESOPHAGEAL FISTULA

♀ 35 yrs.

- HISTORY: DYSPHAGIA WITH COUGHING ON SWALLOWING LIQUIDS. LOSS OF WEIGHT
- PHYSICAL FINDINGS: PNEUMONIA OF RIGHT LUNG

ROENTGEN, ESOPHAGOSCOPY, BRONCHOSCOPY } CONFIRMED CLINICAL DIAGNOSIS OF BRONCHO-ESOPHAGEAL FISTULA

- TREATMENT: SURGICAL REPAIR
- RESULT: CURE

BRONCHOESOPHAGEAL FISTULA

Chart 3.—Bronchoesophageal fistula often is a complication of traction diverticulum secondary to tuberculosis of the tracheobronchial lymph nodes. In our group, two cases were treated successfully by surgical means.

SPONTANEOUS PERFORATION

♂ 50 and 65 yrs.

- HISTORY OF PEPTIC ULCER. DURING VOMITING SEVERE EPIGASTRIC PAIN RADIATING TO BACK
- PHYSICAL FINDINGS: COLLAPSE, RIGIDITY, INHIBITION OF PERISTALSIS, DULLNESS AND RALES IN LEFT CHEST.
- DIAGNOSIS: PERFORATION OF ESOPHAGUS
- TREATMENT: SIMPLE SUTURE OF PERFORATION
- RESULT: RECOVERY

♂ 70 and 58 yrs.

- DEATH SOON AFTER ADMISSION TO HOSPITAL

AUTOPSY:

♂ 70 yrs. PERFORATION 2 CM DIAMETER; ULCER NOT PRESENT

♂ 58 yrs. TWO SMALL ULCERS OF LOWER ESOPHAGUS WITH PERFORATION

SPONTANEOUS PERFORATION OF THE ESOPHAGUS

Chart 4.—In four cases of spontaneous perforation of the esophagus, almost identical history and physical findings led to correct clinical diagnosis. In the two cases in which surgery was applicable, recovery took place.

ESOPHAGEAL STENOSIS 8 cases

Diagnosis is a Problem

Diagnosis	Clinical	Roentgenologic	Esophagoscopic	Pathologic
Benign stenosis	6	5	4	6
Postoperative stenosis	2	1	2	0
Carcinoma	1	1	1	0
Leukoplakia	0	0	0	1
Other esophageal lesion	0	1 (no diagnosis)	1	1 (no diagnosis)

TREATMENT

	Cases	Result: Good	Result: Death
Esophagectomy with esophagogastrostomy	7	5	2
Repeated dilatations	1	1	0

ESOPHAGEAL STENOSIS

Chart 5.—To illustrate the practical problems in esophageal stenosis, the diagnosis made by clinical, roentgenologic, and esophagoscopic methods are compared with the pathologic diagnoses in the accompanying Table. Whereas the method used in the past (repeated dilatation) was utilized in one of the eight cases without mortality, surgical treatment was applied in seven cases with appreciable mortality.

ESOPHAGITIS 17 cases

Diagnosis is a Problem

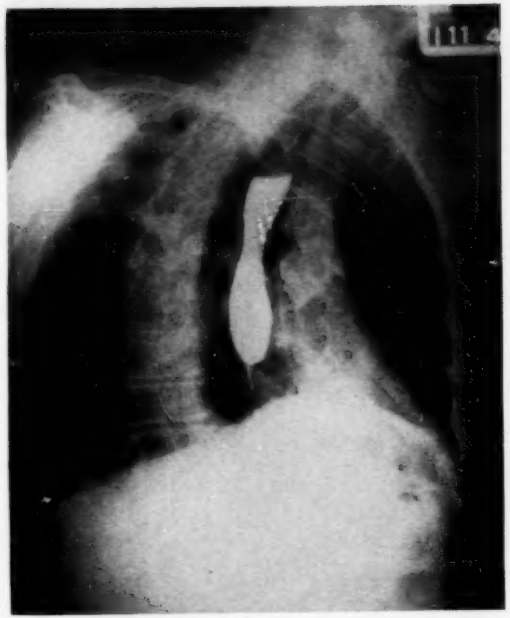
Diagnosis	Clinical	Roentgenologic	Esophagoscopic	Pathologic
Esophagitis	6	6	6	10
Neoplasm	5	2	6	6
Carcinoma	2	1	0	6
Peptic ulcer	2	1	0	0
Hiatal esophagus	2	1	0	0
Abscess	1	0	0	0
Congenital short esophagus	1	0	0	0
Psoriatic arthropathy	0	0	0	1

♀ 58 yrs.

- History of partial gastric resection for duodenal ulcer with obstruction and recent bleeding 5 yrs. previously
- Fluoroscopy revealed delay in distal third of esophagus and small hiatal hernia
- Esophagoscopy disclosed eroded granular mucosa which bled easily
- Biopsy reported acute esophagitis
- Result: spontaneous recovery

ESOPHAGITIS

Chart 6.—Diagnosis is a problem in esophagitis as revealed in the accompanying Table. An illustrative case of postoperative esophagitis is presented.



PEPTIC ULCER

27 cases ♂22 ♀5

SYMPTOMS
EACH PRESENT IN 13 OR 14 CASES

- PAIN
- HEMATEMESIS
- MELENA
- DYSPHAGIA
- REGURGITATION

SIGNS

EPIGASTRIC TENDERNESS	6 CASES
CACHEXIA	6
SHOCK	1
ABSENT	12

Diagnosis is a Problem

Diagnosis	CLINICAL	ROENTGENOLOGIC	ESOPHAGOSCOPIC	AUTOPSY
NO DIAGNOSIS	13	15	17	2
BENIGN ULCER	7	1	6	25
NEOPLASM	6	2	4	1
VARICES (BLEEDING)	1	0	0	0
STENOSIS	0	5	0	0
HIATAL HERNIA	0	3	0	0
ESOPHAGITIS	0	1	0	0

TREATMENT

	CASES	RESULT	
MEDICAL	7	GOOD 4	POOR 3
SURGICAL	7	GOOD 4	POOR 3

♂69 yrs.

- HISTORY: PEPTIC ULCER WITH BLEEDING 15 YEARS PREVIOUSLY. VOMITING OF "ACID", 2 YEARS. DYSPHAGIA AND LOSS OF WEIGHT, 6 MONTHS
- SIGNS: POOR NUTRITIONAL STATE
- LABORATORY FINDINGS: ANEMIA AND 6 UNITS OF FREE HCl.
- X-RAY: STENOSIS DISTAL THIRD OF ESOPHAGUS AND DUODENAL DIVERTICULUM
- ESOPHAGOSCOPY: NARROWING AND IRREGULARITY OF ESOPHAGEAL WALL
- OPERATION: RESECTION WITH ESOPHAGOGASTRIC ANASTOMOSIS
- PATHOLOGY: ULCER 3cm. diameter, CHRONIC PEPTIC ULCER
- RESULT: RECOVERY
- FOLLOW-UP: DEATH 2 YRS. AFTER OPERATION FROM MASSIVE HEMORRHAGE
- AUTOPSY: NOT OBTAINED

PEPTIC ULCER

Chart 7.—Peptic ulcer of the esophagus likewise presents a problem in diagnosis as illustrated in the Table. A variety of presenting symptoms was noted, and frequently there was an absence of physical signs. Medical and surgical treatment was applied in an equal number of patients with comparable results—that is, the good results only slightly outnumbered the poor results.

SUMMARY

OF 18 CASES OF **LEUKOPLAKIA** OF THE ESOPHAGUS, THE CONDITION WAS DIAGNOSED CLINICALLY IN ONLY 2

•

THE CASES OF **BRONCHO-ESOPHAGEAL FISTULA** WERE SUCCESSFULLY TREATED BY SURGERY

•

OF 4 CASES OF **SPONTANEOUS PERFORATION**, 2 WERE TREATED SUCCESSFULLY BY SURGERY

•

OF 7 CASES OF **STENOSIS TREATED SURGICALLY**, 5 WERE SUCCESSFUL

•

OF 17 CASES OF **ESOPHAGITIS** ONLY 6 WERE DIAGNOSED CLINICALLY, THE BALANCE BEING CONFUSED WITH OTHER CONDITIONS

•

PEPTIC ULCER OF THE ESOPHAGUS IS MORE COMMON IN MALES. ESOPHAGOSCOPY WAS THE MOST EFFICIENT METHOD OF DIAGNOSIS AND GOOD RESULTS FROM MEDICAL AND SURGICAL TREATMENT WERE OBTAINED IN AN EQUAL NUMBER OF CASES

SUMMARY

Chart 8.—In the so-called benign conditions of the esophagus, surgical treatment may be applied in a limited number of instances. According to this study, some conditions are more amenable to surgery than others. This emphasizes the fact that in these conditions case individualization is extremely important.

Scientific Exhibits

REGRESSION OF MAMMARY CANCER AFTER ADRENALECTOMY

CHARLES HUGGINS, M.D.
THOMAS L-Y. DAO, M.D.
DELBERT M. BERGENSTAL, M.D.
AND
JOHN LAMBERT SOMMER, M.D.

THE PURPOSE of this exhibit is to demonstrate evidence of some benefits which can occur in patients with metastatic cancer of the breast after bilateral adrenalectomy and to present the principles of medical and surgical management involved in this procedure.

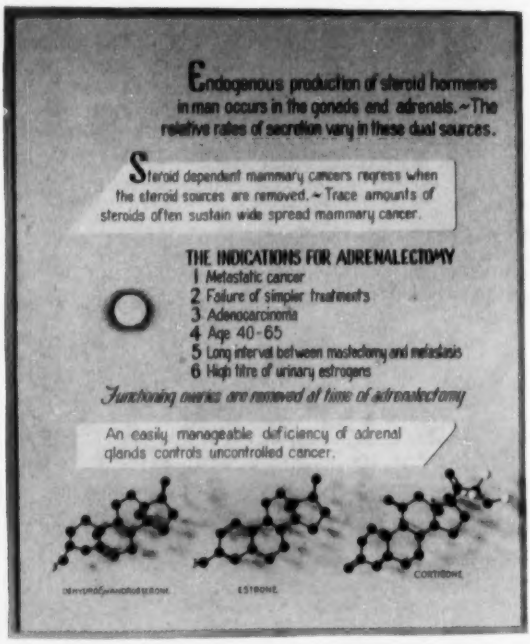

Endogenous production of steroid hormones in man occurs in the gonads and adrenals.~The relative rates of secretion vary in these dual sources.
Steroid dependent mammary cancers regress when the steroid sources are removed.~Trace amounts of steroids often sustain wide spread mammary cancer.
THE INDICATIONS FOR ADRENALECTOMY
1 Metastatic cancer
2 Failure of simpler treatments
3 Adenocarcinoma
4 Age 40-65
5 Long interval between mastectomy and metastasis
6 High titre of urinary estrogens
Functioning ovaries are removed at time of adrenalectomy
An easily manageable deficiency of adrenal glands controls uncontrolled cancer.
ESTRONE
CORTISONE

Fig. 1.—It has been known since the work (1896) of Sir George Beatson in Glasgow that regression of mammary cancer sometimes can be induced by bilateral oöphorectomy. It has been established by recent work that hormones similar to those produced in the ovary are formed in the human adrenal glands as well. The excision of ovaries and adrenal glands is undertaken to eliminate steroids formed in these sources. When mammary cancer in man or woman is steroid-dependent, a striking regression of the disease with long regression of the cancer often occurs after excision of these steroid-producing glands.

From the Ben May Laboratory for Cancer Research and the Department of Medicine, University of Chicago.

Shown as a scientific exhibit of the Section on Surgery, General and Abdominal at the 103rd Annual Meeting of the American Medical Association, San Francisco, June 21-25, 1954.

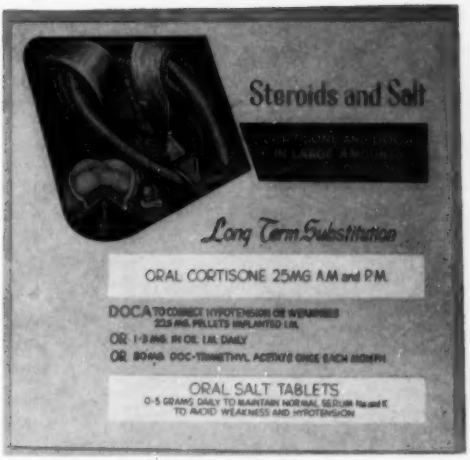
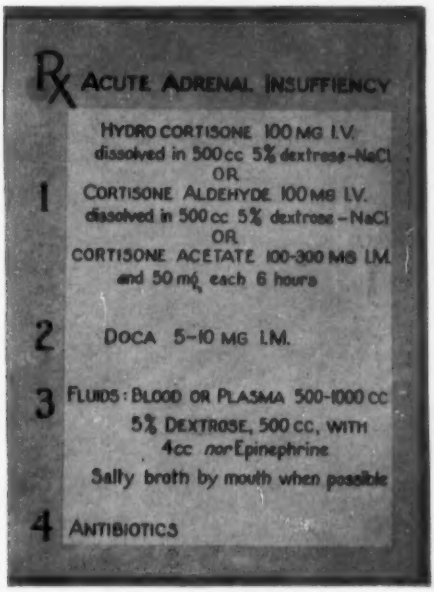

Steroids and Salt
Long Term Substitution
ORAL CORTISONE 25MG A.M. and P.M.
DOCA TO CORRECT HYPOTENSION OR WEAKNESS
OR 1-3 MG. IN OIL I.M. DAILY
ORAL SALT TABLETS
TO AVOID WEAKNESS AND HYPOTENSION

Figure 2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dissolved in 500 cc 5% dextrose-NaCl
OR
1 CORTISONE ALDEHYDE 100 MG I.V.
dissolved in 500 cc 5% dextrose-NaCl
OR
CORTISONE ACETATE 100-300 MG I.M.
and 50 mg. each 6 hours
2 DOCA 5-10 MG I.M.
3 FLUIDS: BLOOD OR PLASMA 500-1000 CC
5% DEXTROSE, 500 CC, WITH
4cc norEpinephrine
Salty broth by mouth when possible
4 ANTIBIOTICS

Figure 3

Fig. 2.—In this clinic, adrenalectomy has been performed only for far advanced mammary cancer in patients who have been subjected to attempts at controlling the disease by simpler measures such as by irradiation, testosterone, or estrogenic substances. When the ovaries are suspected or known to have active physiologic function, regardless of the age of the patient, oöphorectomy is combined in a one-stage operation with adrenalectomy. In our hands a posterolateral incision in the flank gives the best surgical exposure of the adrenals. Since the adrenal glands are essential to life, hormone-substitution must be carried out meticulously. Both the medical and the surgical details of adrenalectomy are demanding; so this procedure must not be embarked upon lightly or in the absence of a good clinical laboratory or of full modern hospital facilities.

Fig. 3.—Needless to say, the physician should be alert to the development of adrenal insufficiency and institute prompt treatment upon the appearance of the first signs of Addisonian crisis.

Fig. 4.—The clinical regression of widespread cancer of the breast is often pleasing to the patient and gratifying to the surgeon. In the first patient treated by adrenalectomy, there was extensive involvement of the skeleton with cancer and many fractured bones. The fractures have healed; the metastases have become stabilized, and the patient is ambulatory three and one-half years after adrenalectomy.

Fig. 5.—Regression of the cancer in osteolytic metastases with regeneration of bone can occur within a few weeks after adrenalectomy.

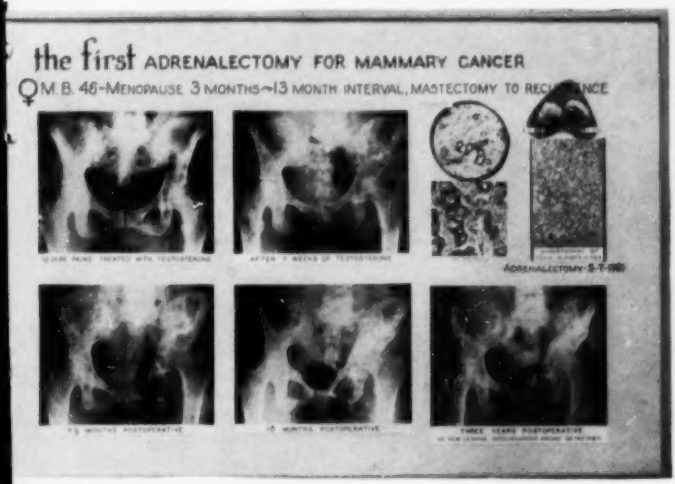
the first ADRENALECTOMY FOR MAMMARY CANCER
♀ M.B. 46-MENOPAUSE 3 MONTHS-13 MONTH INTERVAL, MASTECTOMY TO RECURRENCE
ADRENALECTOMY-5-7-(50)
THREE YEARS POSTOPERATIVE

Figure 4

Speed of Recalcification
OF OSTEOLYTIC METASTASES
AFTER ADRENALECTOMY
♀ G.M. 56 JELLY ARM
♀ M.A. 52 METASTASIS IN TERMINAL PHALANX

Figure 5

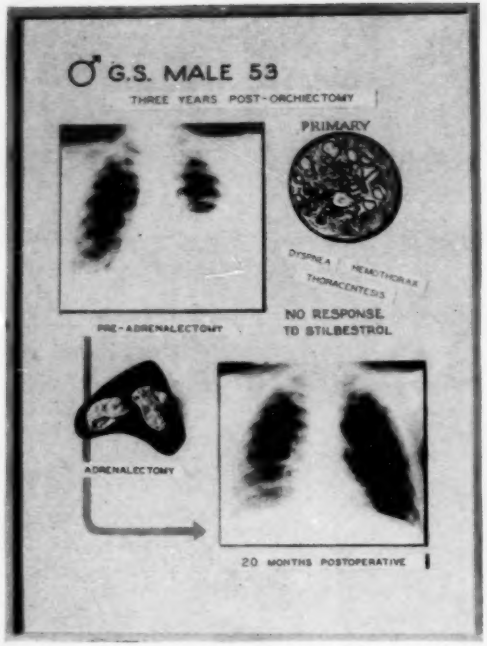

Figure 6

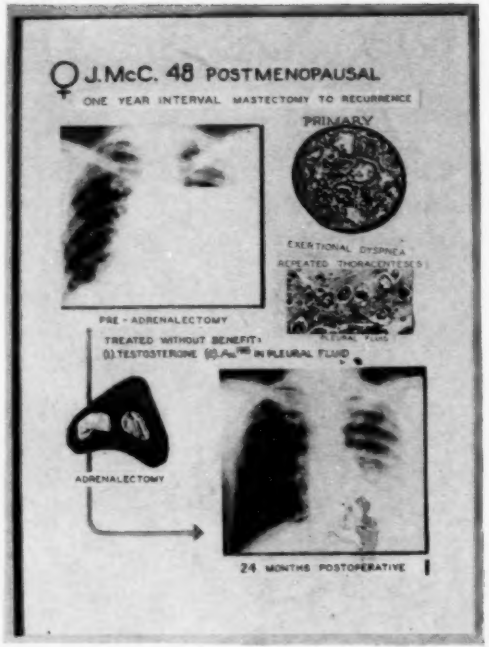

Figure 7

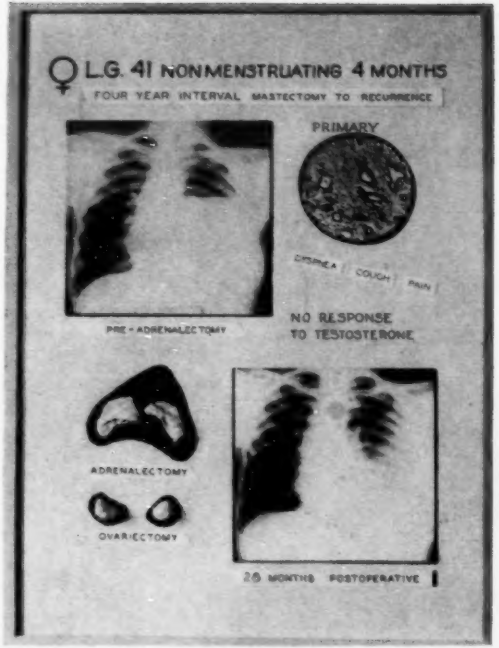

Figure 8

Disappearance of pleural fluid due to metastases in the pleura is often observed as in the three cases shown in Figures 6, 7, and 8.

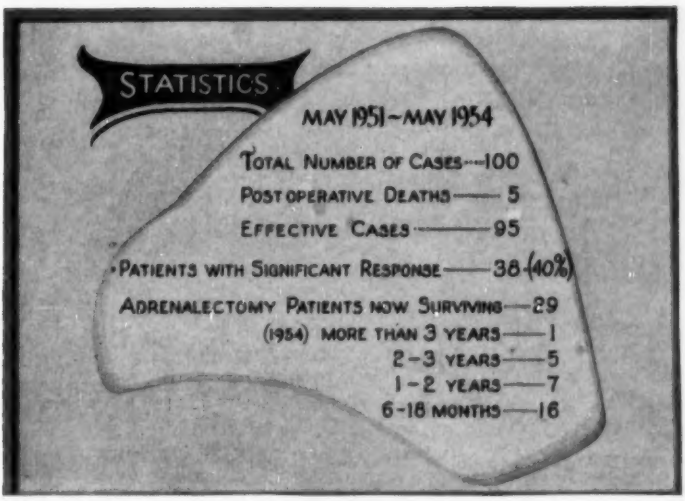

Figure 9

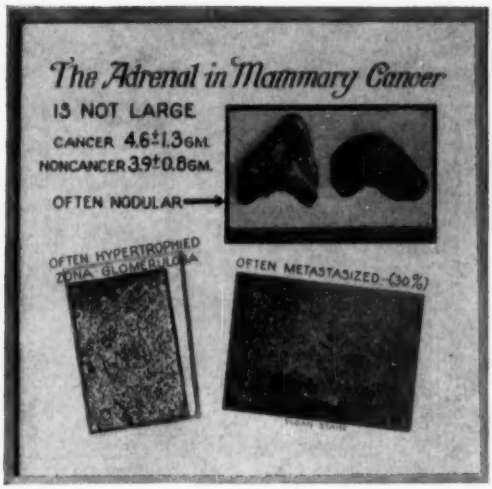

Figure 10

Fig. 10.—The adrenal gland in mammary cancer is usually not enlarged but the cortex is often nodular, and there is frequently hypertrophy of the zona glomerulosa.

Fig. 11.—The histologic appearance of the primary tumor is of importance. Only well differentiated cancer commonly respond to adrenalectomy.

Figure 11

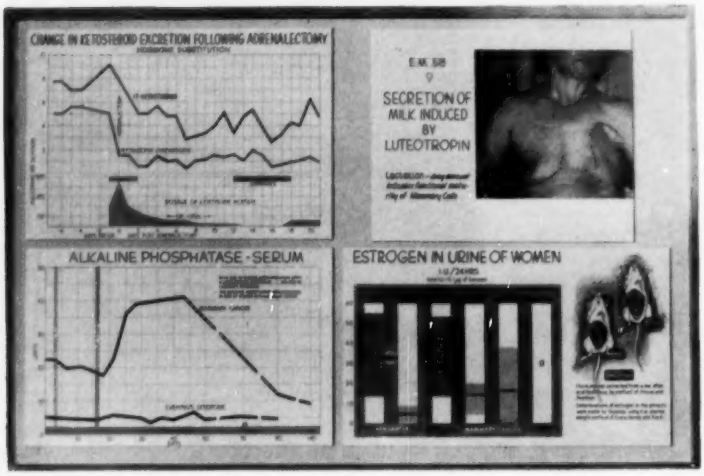
CHANGE IN KETOSTEROID EXCRETION FOLLOWING ADRENALECTOMY
SECRETION OF MILK INDUCED BY LUTEOTROPIN
ALKALINE PHOSPHATASE - SERUM
ESTROGEN IN URINE OF WOMEN

Fig. 12.—A titer of estrogenic substances in the urine above 15 I. U. daily is evidence of significant hormonal production.[1]

We employ four criteria which are helpful in the selection of candidates for adrenalectomy:

1. Age 40 to 65 years.
2. A prolonged interval (more than one year) between radical mastectomy and recurrence of the cancer.
3. Histologic appearance of the primary tumor (Fig. 11).
4. Titer of urinary estrogenic substances above 15 I. U. daily (Fig. 12).

REFERENCE

Huggins, C.: J. Nat. Cancer Inst. **15**:1-25, 1954.

Clinical Notes, New Instruments and Techniques

ESOPHAGEAL TRANSILLUMINATOR

ERNEST B. EMERSON Jr., M.D
ROCHESTER, N. Y.

With the refinement of modern surgical techniques and the advent of sulfonamide and antibiotic therapy, excision of an esophageal diverticulum no longer poses the complicated problems of 10 or more years ago. The esophageal transilluminator is presented as a further refinement and time-saver for a procedure already well established.

The idea of internal illumination of an esophageal diverticulum is not entirely new. Terry [1] sugegsted the use of a flexible Canevon light. Wilson, Wallace, Whiting, and Poole,[2] in 1953. described a lighted probe that would be passed into the diverticulum. As many an endoscopist knows, not infrequently he is called to the operating room to hold an esophageal speculum or esophagoscope in a diverticulum while the surgeon hunts for illusive cleavage planes.

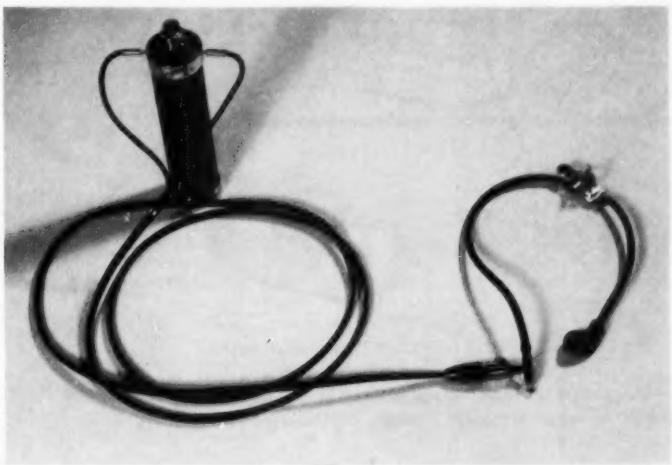

Fig. 1.—Esophageal transilluminator attached to standard cord and battery.

Thus it appears that there is a very definite place for an instrument which would allow transillumination of a diverticulum at the operating table. With the safety factor in mind, the transilluminator herein described is nonrigid so that it may be handled safely by the anesthetist in hospitals when an esophagoscopist is not available. An added advantage of the instrument is that it allows the surgeon, by means of an inlying balloon, to inflate or deflate the diverticulum itself, thereby helping to define cleavage planes and the true extent of the diverticulum itself.

THE INSTRUMENT

The esophageal transilluminator (Fig. 1) consists of essentially three parts. 1. At the peripheral end a small electric light bulb is encased in a balloon. 2. An intervening electric cord is

From the Department of Surgery, Division of Otolaryngology, University of Rochester School of Medicine and Dentistry.

encased within a rubber tube. 3. At the proximal end a fitting is attached which allows the use of a standard battery circuit available in most operating rooms and a bulb for inflating the peripheral balloon via the intervening rubber tube.

TECHNIQUE

The technique of insertion of the instrument will present no great problem to the trained endoscopist. If no esophagoscopist is available, the method of choice is first to insert an intratracheal anesthesia tube. Once this has been done, the transilluminator may be passed blind into the diverticulum by the anesthetist and, because of its nonrigid construction, danger of perforation will be minimal. The balloon may then be inflated and the light switched on in any manner that fits the requirements of the surgeon (Fig. 2).

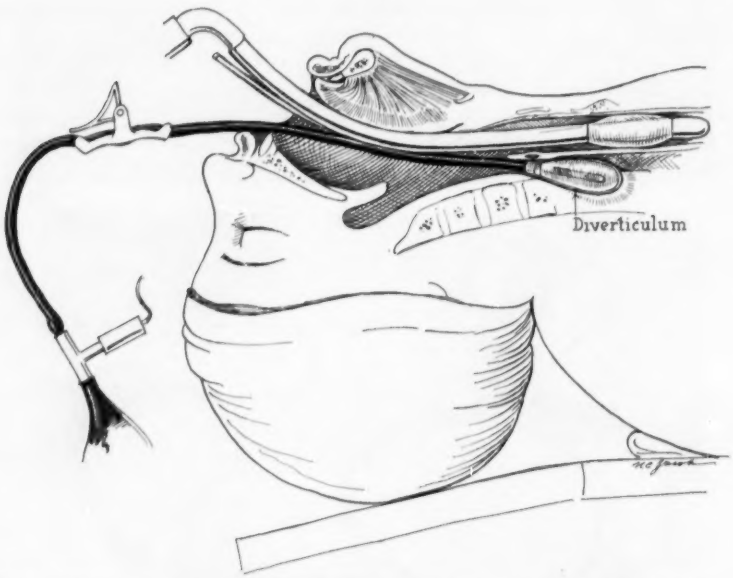

Fig. 2.—Diagrammatic drawing showing an intratrachial tube in place and the esophageal transilluminator in the diverticulum partially inflated.

SUMMARY

An esophageal transilluminator is presented.

The instrument has been found satisfactory for the purpose for which it was designed, i. e., transillumination and inflation of an esophageal diverticulum during its excision.

The nonrigid character of the instrument plus the advantage of being able to inflate the diverticulum by means of a balloon makes the instrument desirable from the point of view both of safety and of shortening operating time.

The esophageal transilluminator is available to physicians at Welch & Allyn, Inc., Skaneateles Falls, N. Y.

REFERENCES

1. Terry, R. N.: Oesophageal Intubation for Repair of Pharyngeo-Esophageal Diverticulum, Am. J. Surg. **80**:338-340 (Sept.) 1950.

2. Wilson, R. S.; Wallace, F. T.; Whiting, J. A., and Poole, C. H.: Technical Aid in Esophageal Diverticulectomy **22**:192-195 (Aug.) 1953

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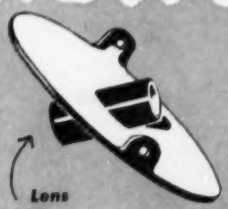

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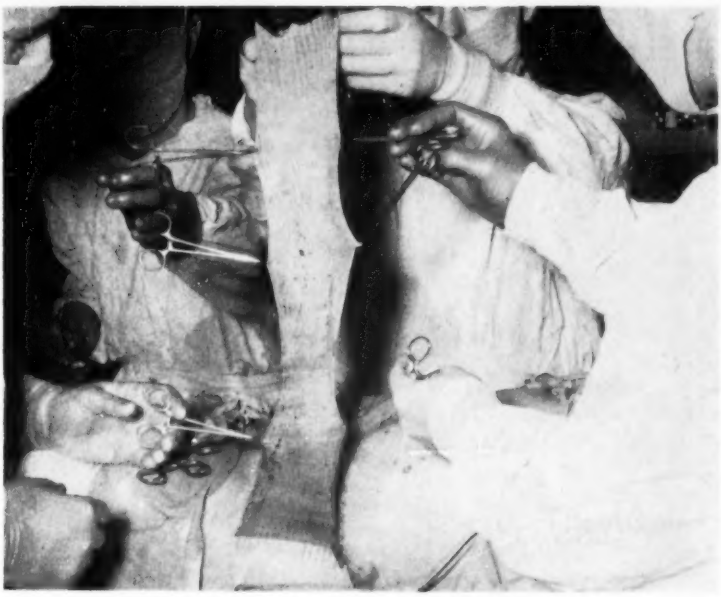

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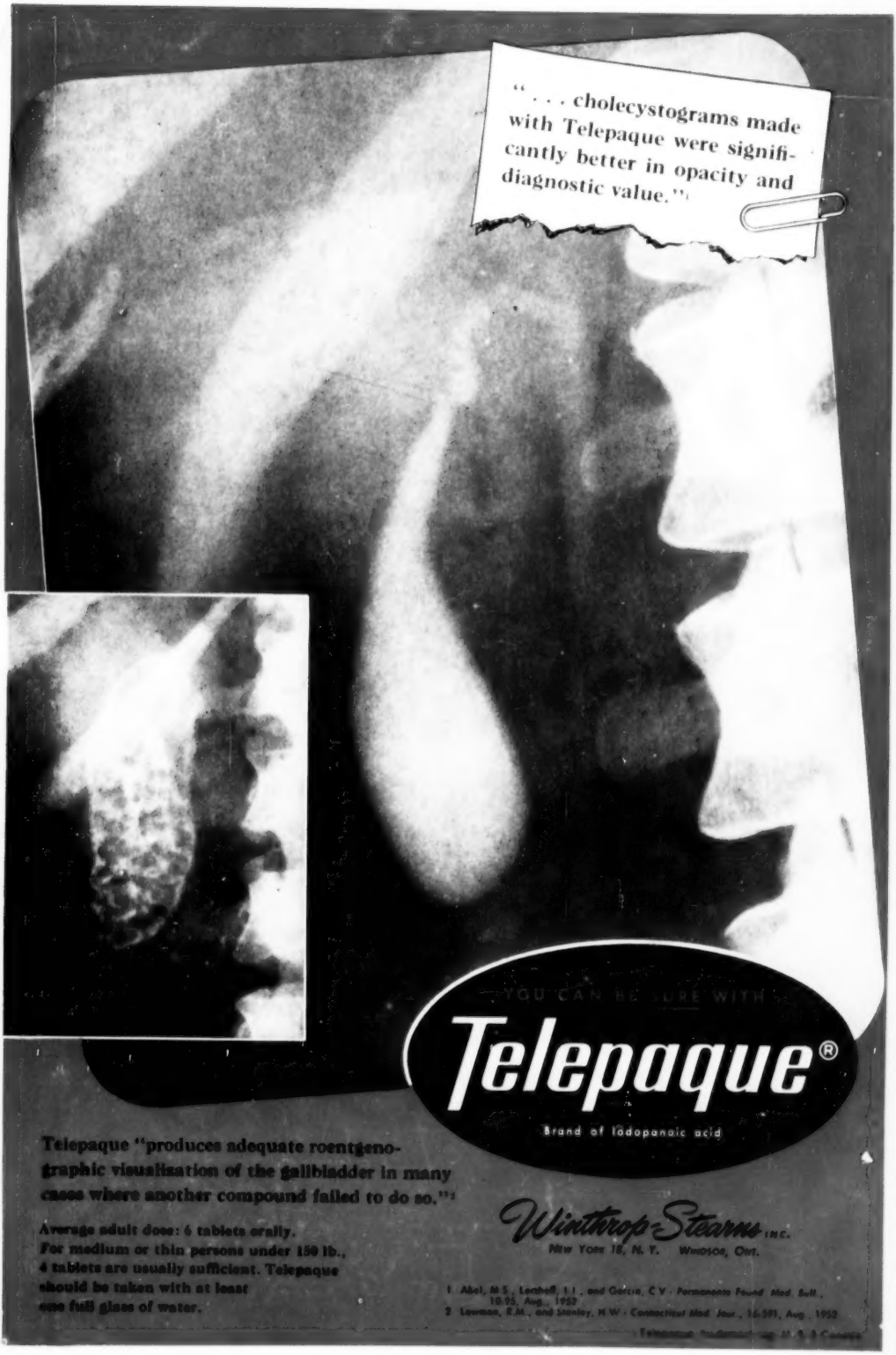
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1. Abel, M.S., Lenhoff, I.I., and Garcia, C.V.: Permanente Found. Med. Bull., 10:95, Aug., 1952
2. Lawson, R.M., and Stanley, H.W.: Connecticut Med. Jour., 16:591, Aug., 1952

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